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**COMMISSION REGULATION (EU) No 546/2011**

**of 10 June 2011**

**implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products**

**(Text with EEA relevance)**

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*Article 1*

The uniform principles for evaluation and authorisation of plant protection products provided for in Article 29(6) of Regulation (EC) No 1107/2009 shall be as set out in the Annex to this Regulation.

*Article 2*

This Regulation shall enter into force on the 20th day following its publication in the *Official Journal of the European Union*.

It shall apply from 14 June 2011.

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

*ANNEX***UNIFORM PRINCIPLES FOR EVALUATION AND AUTHORISATION  
OF PLANT PROTECTION PRODUCTS, AS PROVIDED FOR IN  
ARTICLE 29(6) OF REGULATION (EC) No 1107/2009****PART I****Uniform principles for evaluation and authorisation of chemical plant  
protection products**

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## A. INTRODUCTION

1. The principles developed in this Annex aim to ensure that evaluations and decisions with regard to authorisation of plant protection products, provided they are chemical preparations, results in the implementation of the requirements of Article 29(1)(e) in conjunction with Article 4(3) and Article 29(1)(f), (g) and (h) of Regulation (EC) No 1107/2009 by all the Member States at a high level of protection of human and animal health and the environment.
2. In evaluating applications and granting authorisations Member States shall:
  - (a) — ensure that the dossier supplied is in accordance with the requirements of the Annex to Commission Regulation (EU) No 545/2011 <sup>(1)</sup>, at the latest at the time of finalisation of the evaluation for the purpose of decision-making, without prejudice, where relevant, to the provisions of Articles 33, 34 and 59 of Regulation (EC) No 1107/2009,
    - ensure that the data submitted are acceptable in terms of quantity, quality, consistency and reliability and sufficient to permit a proper evaluation of the dossier,
    - evaluate, where relevant, justifications submitted by the applicant for not supplying certain data;
  - (b) take into account the data concerning the active substance in the plant protection product of the Annex to Commission Regulation (EU) No 544/2011 <sup>(2)</sup>, submitted for the purpose of approval of the active substance under Regulation (EC) No 1107/2009, and the results of the evaluation of those data, without prejudice, where relevant, to the provisions of Article 33(3) and Articles 34 and 59 of Regulation (EC) No 1107/2009;
  - (c) take into consideration other relevant technical or scientific information they can reasonably possess with regard to the performance of the plant protection product or to the potentially adverse effects of the plant protection product, its components or its residues.
3. Where in the specific principles on evaluation reference is made to data of the Annex to Regulation (EU) No 544/2011, this shall be understood as being the data referred to in point 2 (b).
4. Where the data and information provided are sufficient to permit completion of the evaluation for one of the proposed uses, applications must be evaluated and a decision made for the proposed use.

Taking account of justifications provided and with the benefit of any subsequent clarifications, Member States shall reject applications for which the data gaps are such that it is not possible to finalise the evaluation and to make a reliable decision for at least one of the proposed uses.

5. During the process of evaluation and decision-making, Member States shall cooperate with the applicants in order to resolve any questions on the dossier quickly or to identify at an early stage any additional studies necessary for a proper evaluation of the dossier, or to amend any proposed conditions for the use of the plant protection product or to modify its nature or its composition in order to ensure full satisfaction of the requirements of this Annex or of Regulation (EC) No 1107/2009.

Member States shall come to a reasoned decision within 12 months of receiving a technically complete dossier. A technically complete dossier is one that satisfies all the requirements of the Annex to Regulation (EU) No 545/2011.

<sup>(1)</sup> See page 67 of this Official Journal.

<sup>(2)</sup> See page 1 of this Official Journal.

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6. The judgements made by the competent authorities of the Member States during the evaluation and decision-making process must be based on scientific principles, preferably recognised at international level (for example, by the EPPO), and be made with the benefit of expert advice.

**B. EVALUATION****1. General principles**

- 1.1. Having regard to current scientific and technical knowledge, Member States shall evaluate the information referred to in point 2 of Part A and in particular:

- (a) assess the performance in terms of efficacy and phytotoxicity of the plant protection product for each use for which authorisation is sought; and
- (b) identify the hazard arising, assess their significance and make a judgment as to the likely risks to humans, animals or the environment.

- 1.2. In accordance with the terms of Article 29 of Regulation (EC) No 1107/2009, which, *inter alia*, specifies that Member States shall have regard to all normal conditions under which the plant protection product may be used, and to the consequences of its use, Member States shall ensure that evaluations carried out have regard to the proposed practical conditions of use and in particular to the purpose of use, the dose, the manner, frequency and timing of applications, and the nature and composition of the preparation. Whenever possible Member States shall also take into account the principles of integrated control.

- 1.3. In the evaluation of applications submitted, Member States shall have regard to the agricultural, plant health or environmental (including climatic) conditions in the areas of use.

- 1.4. In interpreting the results of evaluations, Member States shall take into consideration possible elements of uncertainty in the information obtained during the evaluation, in order to ensure that the chances of failing to detect adverse effects or of under-estimating their importance are reduced to a minimum. The decision-making process shall be examined to identify critical decision points or items of data for which uncertainties could lead to a false classification of risk.

The first evaluation made shall be based on the best available data or estimates reflecting the realistic conditions of use of the plant protection product.

This should be followed by a repeat evaluation, taking account of potential uncertainties in the critical data and of a range of use conditions that are likely to occur and resulting in a realistic worst-case approach, to determine whether it is possible that the initial evaluation could have been significantly different.

- 1.5. Where specific principles of Section 2 provide for the use of calculation models in the evaluation of a plant protection product, those models shall:

- make a best possible estimation of all relevant processes involved taking into account realistic parameters and assumptions,
- be submitted to an analysis as referred to in B, point 1.4,
- 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.

- 1.6. Where metabolites, degradation or reaction products are referred to in the specific principles, only those that are relevant for the proposed criterion shall be taken into consideration.

**▼B****2. Specific principles**

Member States shall, for the evaluation of the data and information submitted in support of applications, and without prejudice to the general principles of Section 1, implement the following principles.

**2.1. Efficacy**

2.1.1. Where the proposed use concerns the control of or protection against an organism, Member States shall evaluate the possibility that this organism could be harmful under the agricultural, plant health and environmental (including climatic) conditions in the area of the proposed use.

2.1.2. Where the proposed use concerns an effect other than the control of or protection against an organism, Member States shall evaluate whether significant damage, loss or inconvenience could occur under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use if the plant protection product were not used.

2.1.3. Member States shall evaluate the efficacy data on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011 having regard to the degree of control or the extent of the effect desired and having regard to the relevant experimental conditions such as:

- the choice of the crop or cultivar,
- the agricultural and environmental (including climatic) conditions,
- the presence and density of the harmful organism,
- the development stage of crop and organism,
- the amount of the plant protection product used,
- if required on the label, the amount of adjuvant added,
- the frequency and timing of the applications,
- the type of application equipment.

2.1.4. Member States shall evaluate the performance of the plant protection product in a range of agricultural, plant health and environmental (including climatic) conditions likely to be encountered in practice in the area of proposed use and in particular:

- (i) the level, consistency and duration of the effect sought in relation to the dose in comparison with a suitable reference product or products and an untreated control;
- (ii) where relevant, effect on yield or reduction of loss in storage, in terms of quantity and/or quality, in comparison with a suitable reference product or products and an untreated control.

Where no suitable reference product exists, Member States shall evaluate the performance of the plant protection product to determine whether there is a consistent and defined benefit under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

2.1.5. 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, Member States shall make the evaluations referred to in points 2.1.1 to 2.1.4 in relation to the information supplied for the tank mix.

Where the product label includes recommendations for use of the plant protection product with other plant protection products and/or with adjuvants as a tank mix, Member States shall evaluate the appropriateness of the mix and of its conditions of use.

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- 2.2. *Absence of unacceptable effects on plants or plant products*
- 2.2.1. Member States shall evaluate the degree of adverse effects on the treated crop after use of the plant protection product in accordance with the proposed conditions of use in comparison, where relevant, with a suitable reference product or products, where they exist, and/or an untreated control.
- (a) This evaluation shall take into consideration the following information:
- (i) the efficacy data provided for in the Annex to Regulation (EU) No 545/2011;
  - (ii) other relevant information on the plant protection product such as nature of the preparation, dose, method of application, number and timing of applications;
  - (iii) all relevant information on the active substance as provided for in of the Annex to Regulation (EU) No 544/2011, including mode of action, vapour pressure, volatility and water solubility.
- (b) This evaluation shall include:
- (i) the nature, frequency, level and duration of observed phytotoxic effects and the agricultural, plant health and environmental (including climatic) conditions that affect them;
  - (ii) the differences between main cultivars with regard to their sensitivity to phytotoxic effects;
  - (iii) the part of the treated crop or plant products where phytotoxic effects are observed;
  - (iv) the adverse impact on the yield of the treated crop or plant products in terms of quantity and/or quality;
  - (v) the adverse impact on treated plants or plant products to be used for propagation, in terms of viability, germination, sprouting, rooting and establishment;
  - (vi) where volatile products are concerned, the adverse impact on adjacent crops.
- 2.2.2. Where the available data indicate that the active substance or significant metabolites, degradation and reaction products persist in soils and/or in or on plant substances in significant quantities after use of the plant protection product in accordance with the proposed conditions of use, Member States shall evaluate the degree of adverse effects on subsequent crops. This evaluation shall be carried out as specified in point 2.2.1.
- 2.2.3. 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 evaluation as specified in point 2.1.1 shall be carried out in relation to the information supplied for the tank mix.
- 2.3. *Impact on vertebrates to be controlled*
- Where the proposed use of the plant protection product aims to have an effect on vertebrates, Member States shall evaluate the mechanism by which this effect is obtained and the observed effects on the behaviour and health of the target animals; when the intended effect is to kill the target animal they shall evaluate the time necessary to obtain the death of the animal and the conditions under which death occurs.

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This evaluation shall take into consideration the following information:

- (i) all relevant information as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof, including the toxicological and metabolism studies;
- (ii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011, including toxicological studies and efficacy data.

2.4. *Impact on human or animal health*

2.4.1. Impact on human or animal health arising from the plant protection product

2.4.1.1. Member States shall evaluate operator exposure to the active substance and/or to toxicologically relevant compounds in the plant protection product likely to occur under the proposed conditions of use (including in particular dose, application method and climatic conditions) using by preference realistic data on exposure and, if such data are not available, a suitable, validated calculation model.

(a) This evaluation shall take into consideration the following information:

(i) the toxicological and metabolism studies as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof including the acceptable operator exposure level (AOEL). The acceptable operator exposure level is the maximum amount of active substance to which the operator may be exposed without any adverse health effects. The AOEL is expressed as milligrams of the chemical per kilogram body weight of the operator. The AOEL is based on the highest level at which no adverse effect is observed in tests in the most sensitive relevant animal species or, if appropriate data are available, in humans;

(ii) other relevant information on the active substances such as physical and chemical properties;

(iii) the toxicological studies provided for in the Annex to Regulation (EU) No 545/2011, including where appropriate dermal absorption studies;

(iv) other relevant information as provided for in the Annex to Regulation (EU) No 545/2011 such as:

- composition of the preparation,
- nature of the preparation,
- size, design and type of packaging,
- field of use and nature of crop or target,
- method of application including handling, loading and mixing of product,
- exposure reduction measures recommended,
- protective clothing recommendations,
- maximum application rate,
- minimum spray application volume stated on the label,
- number and timing of applications.

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- (b) This evaluation shall be made for each type of application method and application equipment proposed for use of the plant protection product as well as for the different types and sizes of containers to be used, taking account of mixing, loading operations, application of the plant protection product and cleaning and routine maintenance of application equipment.

2.4.1.2. Member States shall examine information relating to the nature and characteristics of the packaging proposed with particular reference to the following aspects:

- the type of packaging,
- its dimensions and capacity,
- the size of the opening,
- the type of closure,
- its strength, leakproofness and resistance to normal transport and handling,
- its resistance to and compatibility with the contents.

2.4.1.3. Member States shall examine the nature and characteristics of the protective clothing and equipment proposed with particular reference to the following aspects:

- obtainability and suitability,
- ease of wearing taking into account physical stress and climatic conditions.

2.4.1.4. Member States shall evaluate the possibility of exposure of other humans (bystanders or workers exposed after the application of the plant protection product) or animals to the active substance and/or to other toxicologically relevant compounds in the plant protection product under the proposed conditions of use.

This evaluation shall take into consideration the following information:

- (i) the toxicological and metabolism studies on the active substance as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof, including the acceptable operator exposure level;
- (ii) the toxicological studies provided for in the Annex to Regulation (EU) No 545/2011, including where appropriate dermal absorption studies;
- (iii) other relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011 such as:
  - re-entry periods, necessary waiting periods or other precautions to protect humans and animals,
  - method of application, in particular spraying,
  - maximum application rate,
  - maximum spray application volume,
  - composition of the preparation,
  - excess remaining on plants and plant products after treatment,
  - further activities whereby workers are exposed.

**▼B****2.4.2. Impact on human or animal health arising from residues**

2.4.2.1. Member States shall evaluate the specific information on toxicology as provided for in the Annex to Regulation (EU) No 544/2011 and in particular:

- the determination of an acceptable daily intake (ADI),
- the identification of metabolites, degradation and reaction products in treated plants or plant products,
- behaviour of residues of the active substance and its metabolites from the time of application until harvest, or in the case of post-harvest uses, until outloading of stored plant products.

2.4.2.2. Prior to evaluating the residue levels in the reported trials or in products of animal origin Member States shall examine the following information:

- data on the proposed good agricultural practice, including data on application as provided for in the Annex to Regulation (EU) No 545/2011 and proposed pre-harvest intervals for envisaged uses, or withholding periods or storage periods, in the case of post-harvest uses,
- nature of the preparation,
- analytical methods and the residue definition.

2.4.2.3. On the basis of suitable statistical models Member States shall evaluate the residue levels observed in the reported trials. This evaluation shall be made for each proposed use and shall take into consideration:

- (i) the proposed conditions of use of the plant protection product;
- (ii) the specific information on residues in or on treated plants, plant products, food and feed as provided for in the Annex to Regulation (EU) No 545/2011 and the distribution of residues between edible and non-edible parts;
- (iii) the specific information on residues in or on treated plants, plant products, food and feed as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;
- (iv) the realistic possibilities of extrapolating data from one crop to another.

2.4.2.4. Member States shall evaluate the residue levels observed in products of animal origin, taking into consideration the information provided for in point 8.4 of Part A of the Annex to Regulation (EU) No 545/2011 and residues resulting from other uses.

2.4.2.5. Member States shall estimate the potential exposure of consumers through diet and, where relevant, other ways of exposure, using a suitable calculation model. This evaluation shall take account, where relevant, of other sources of information such as other authorised uses of plant protection products containing the same active substance or which give rise to the same residues.

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2.4.2.6. Member States shall, where relevant, estimate the exposure of animals, taking into account the residue levels observed in treated plants or plant products intended to be fed to animals.

2.5. *Influence on the environment*

2.5.1. Fate and distribution in the environment

In the evaluation of the fate and distribution of the plant protection product in the environment, Member States shall have regard to all aspects of the environment, including biota, and in particular to the following:

2.5.1.1. Member States shall evaluate the possibility of the plant protection product reaching the soil under the proposed conditions of use; if this possibility exists they shall estimate the rate and the route of degradation in the soil, the mobility in the soil and the change in the total concentration (extractable and non-extractable<sup>(1)</sup>) of the active substance and of relevant metabolites, degradation and reaction products that could be expected in the soil in the area of envisaged use after use of the plant protection product in accordance with the proposed conditions of use.

This evaluation shall take into consideration the following information:

- (i) the specific information on fate and behaviour in soil as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
  - molecular weight,
  - solubility in water,
  - octanol/water partition coefficient,
  - vapour pressure,
  - volatilisation rate,
  - dissociation constant,
  - photodegradation rate and identity of breakdown products,
  - hydrolysis rate in relation to pH and identity of breakdown products;
- (iii) all information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011, including the information on distribution and dissipation in soil;
- (iv) where relevant, other authorised uses of plant protection products in the area of proposed use containing the same active substance or which give rise to the same residues.

2.5.1.2. Member States shall evaluate the possibility of the plant protection product reaching the groundwater under the proposed conditions of use; if this possibility exists, they shall estimate, using a suitable calculation model validated at EU level, the concentration of the active substance and of relevant metabolites, degradation and reaction products that could be expected in the groundwater in the area of envisaged use after use of the plant protection product in accordance with the proposed conditions of use.

<sup>(1)</sup> Non-extractable residues (sometimes referred to as 'bound' or 'non-extracted' residues) in plants and soils are defined as chemical species originating from pesticides used in accordance with good agricultural practice that cannot be extracted by methods which do not significantly change the chemical nature of these residues. These non-extractable residues are not considered to include fragments through metabolic pathways leading to natural products.

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As long as there is no validated EU calculation model, Member States shall base their evaluation especially on the results of mobility and persistence in soil studies as provided for in the Annex to Regulation (EU) No 544/2011 and Regulation (EU) No 545/2011.

This evaluation shall also take into consideration the following information:

- (i) the specific information on fate and behaviour in soil and water as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
  - molecular weight,
  - solubility in water,
  - octanol/water partition coefficient,
  - vapour pressure,
  - volatilisation rate,
  - hydrolysis rate in relation to pH and identity of breakdown products,
  - dissociation constant;
- (iii) all information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011, including the information on distribution and dissipation in soil and water;
- (iv) where relevant, other authorised uses of plant protection products in the area of envisaged use containing the same active substance or which give rise to the same residues;
- (v) where relevant, data on dissipation including transformation and sorption in the saturated zone;
- (vi) where relevant, data on the procedures for drinking water abstraction and treatment in the area of envisaged use;
- (vii) where relevant, monitoring data on the presence or absence of the active substance and relevant metabolites, degradation or reaction products in groundwater as a result of previous use of plant protection products containing the same active substance or which give rise to the same residues; such monitoring data shall be interpreted in a consistent scientific way.

2.5.1.3. Member States shall evaluate the possibility of the plant protection product reaching surface water under the proposed conditions of use; if this possibility exists they shall estimate, using a suitable calculation model validated at EU level, the short-term and long-term predicted concentration of the active substance and of metabolites, degradation and reaction products that could be expected in the surface water in the area of envisaged use after use of the plant protection product in accordance with the proposed conditions of use.

If there is no validated EU calculation model, Member States shall base their evaluation especially on the results of mobility and persistence in soil studies and the information on run-off and drift as provided for in the Annex to Regulation (EU) No 544/2011 and to Regulation (EU) No 545/2011.

This evaluation shall also take into consideration the following information:

- (i) the specific information on fate and behaviour in soil and water as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;

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- (ii) other relevant information on the active substance such as:
  - molecular weight,
  - solubility in water,
  - octanol/water partition coefficient,
  - vapour pressure,
  - volatilisation rate,
  - hydrolysis rate in relation to pH and identity of breakdown products,
  - dissociation constant;
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011, including the information on distribution and dissipation in soil and water;
- (iv) possible routes of exposure:
  - drift,
  - run-off,
  - overspray,
  - discharge via drains,
  - leaching,
  - deposit in the atmosphere;
- (v) where relevant, other authorised uses of plant protection products in the area of envisaged use containing the same active substance or which give rise to the same residues;
- (vi) where relevant, data on the procedures for drinking water abstraction and treatment in the area of envisaged use.

2.5.1.4. Member States shall evaluate the possibility of the plant protection product being dissipated in the air under the proposed conditions of use; if this possibility exists they shall make the best possible estimation, using where appropriate a suitable, validated calculation model, of the concentration of the active substance and of relevant metabolites, degradation and reaction products that could be expected in the air after use of the plant protection product in accordance with the proposed conditions of use.

This evaluation shall take into consideration the following information:

- (i) the specific information on fate and behaviour in soil, water and air as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
  - vapour pressure,
  - solubility in water,
  - hydrolysis rate in relation to pH and identity of breakdown products,
  - photochemical degradation in water and air and identity of breakdown products,
  - octanol/water partition coefficient;
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011, including the information on distribution and dissipation in air.

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2.5.1.5. Member States shall evaluate the procedures for destruction or decontamination of the plant protection product and its packaging.

2.5.2. **Impact on non-target species**

When calculating toxicity/exposure ratios Member States shall take into consideration toxicity to the most sensitive relevant organism used in the tests.

2.5.2.1. Member States shall evaluate the possibility of exposure of birds and other terrestrial vertebrates to the plant protection product under the proposed conditions of use; if this possibility exists they shall evaluate the extent of the short-term and long-term risk to be expected for these organisms, including their reproduction, after use of the plant protection product in accordance with the proposed conditions of use.

(a) This evaluation shall take into consideration the following information:

(i) the specific information relating to toxicological studies on mammals and to the effects on birds and other non-target terrestrial vertebrates, including effects on reproduction, and other relevant information concerning the active substance as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;

(ii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011, including the information on effects on birds and other non-target terrestrial vertebrates;

(iii) where relevant, other authorised uses of plant protection products in the area of envisaged use containing the same active substance or which give rise to the same residues.

(b) This evaluation shall include:

(i) the fate and distribution, including persistence and bioconcentration, of the active substance and of relevant metabolites, breakdown and reaction products in the various parts of the environment after application of the plant protection product;

(ii) the estimated exposure of the species likely to be exposed at the time of application or during the period that residues are present, taking into account all relevant routes of exposure such as ingestion of the formulated product or treated food, predation on invertebrates, feeding on vertebrate prey, contact by overspraying or with treated vegetation;

(iii) a calculation of the acute, short-term and, where necessary, long-term toxicity/exposure ratio. The toxicity/exposure ratios are defined as respectively the quotient of LD<sub>50</sub>, LC<sub>50</sub> or non-observable effects of concentration (NOEC) expressed on an active substance basis and the estimated exposure expressed in mg/kg body weight.

2.5.2.2. Member States shall evaluate the possibility of exposure of aquatic organisms to the plant protection product under the proposed conditions of use; if this possibility exists they shall evaluate the degree of short-term and long-term risk to be expected for aquatic organisms after use of the plant protection product in accordance with the proposed conditions of use.

(a) This evaluation shall take into consideration the following information:

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- (i) the specific information relating to the effects on aquatic organisms as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
  - solubility in water,
  - octanol/water partition coefficient,
  - vapour pressure,
  - volatilisation rate,
  - KOC,
  - biodegradation in aquatic systems and in particular the ready biodegradability,
  - photodegradation rate and identity of breakdown products,
  - hydrolysis rate in relation to pH and identity of breakdown products;
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011 and in particular the effects on aquatic organisms;
- (iv) where relevant, other authorised uses of plant protection products in the area of envisaged use, containing the same active substance or which give rise to the same residues.

(b) This evaluation shall include:

- (i) the fate and distribution of residues of the active substance and of relevant metabolites, breakdown and reaction products in water, sediment or fish;
- (ii) a calculation of the acute toxicity/exposure ratio for fish and Daphnia. This ratio is defined as the quotient of respectively acute LC<sub>50</sub> or EC<sub>50</sub> and the predicted short-term environmental concentration;
- (iii) a calculation of the algal growth inhibition/exposure ratio for algae. This ratio is defined as the quotient of the EC<sub>50</sub> and the predicted short-term environmental concentration;
- (iv) a calculation of the long-term toxicity/exposure ratio for fish and Daphnia. The long-term toxicity/exposure ratio is defined as the quotient of the NOEC and the predicted long-term environmental concentration;
- (v) where relevant, the bioconcentration in fish and possible exposure of predators of fish, including humans;
- (vi) if the plant protection product is to be applied directly to surface water, the effect on the change of surface water quality, such as pH or dissolved oxygen content.

2.5.2.3. Member States shall evaluate the possibility of exposure of honeybees to the plant protection product under the proposed conditions of use; if this possibility exists they shall evaluate the short-term and long-term risk to be expected for honeybees after use of the plant protection product in accordance with the proposed conditions of use.

(a) This evaluation shall take into consideration the following information:

- (i) the specific information on toxicity to honeybees as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;

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- (ii) other relevant information on the active substance such as:
  - solubility in water,
  - octanol/water partition coefficient,
  - vapour pressure,
  - photodegradation rate and identity of breakdown products,
  - mode of action (e. g. insect growth regulating activity);
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011, including the toxicity to honeybees;
- (iv) where relevant, other authorised uses of plant protection products in the area of envisaged use, containing the same active substance or which give rise to the same residues.

(b) This evaluation shall include:

- (i) the ratio between the maximum application rate expressed in grams of active substance per hectare and the contact and oral LD<sub>50</sub> expressed in µg of active substance per bee (hazard quotients) and where necessary the persistence of residues on or, where relevant, in the treated plants;
- (ii) where relevant, the effects on honeybee larvae, honeybee behaviour, colony survival and development after use of the plant protection product in accordance with the proposed conditions of use.

2.5.2.4. Member States shall evaluate the possibility of exposure of beneficial arthropods other than honeybees to the plant protection product under the proposed conditions of use; if this possibility exists they shall assess the lethal and sublethal effects on these organisms to be expected and the reduction in their activity after use of the plant protection product in accordance with the proposed conditions of use.

This evaluation shall take into consideration the following information:

- (i) the specific information on toxicity to honeybees and other beneficial arthropods as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;
- (ii) other relevant information on the active substance such as:
  - solubility in water,
  - octanol/water partition coefficient,
  - vapour pressure,
  - photodegradation rate and identity of breakdown products,
  - mode of action (e. g. insect growth regulating activity);
- (iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011 such as:
  - effects on beneficial arthropods other than bees,

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- toxicity to honeybees,
  - available data from biological primary screening,
  - maximum application rate,
  - maximum number and timetable of applications;
- (iv) where relevant, other authorised uses of plant protection products in the area of envisaged use, containing the same active substance or which give rise to the same residues.

2.5.2.5. Member States shall evaluate the possibility of exposure of earthworms and other non-target soil macro-organisms to the plant protection product under the proposed conditions of use; if this possibility exists they shall evaluate the degree of short-term and long-term risk to be expected to these organisms after use of the plant protection product in accordance with the proposed conditions of use.

(a) This evaluation shall take into consideration the following information:

(i) the specific information relating to the toxicity of the active substance to earthworms and to other non-target soil macro-organisms as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;

(ii) other relevant information on the active substance such as:

- solubility in water,
- octanol/water partition coefficient,
- $K_d$  for adsorption,
- vapour pressure,
- hydrolysis rate in relation to pH and identity of breakdown products,
- photodegradation rate and identity of breakdown products,
- DT50 and DT90 for degradation in the soil;

(iii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011, including the effects on earthworms and other non-target soil macro-organisms;

(iv) where relevant, other authorised uses of plant protection products in the area of envisaged use, containing the same active substance or which give rise to the same residues.

(b) This evaluation shall include:

- (i) the lethal and sublethal effects;
- (ii) the predicted initial and long-term environmental concentration;
- (iii) a calculation of the acute toxicity/exposure ratio (defined as the quotient of  $LC_{50}$  and predicted initial environmental concentration) and of the long-term toxicity/exposure ratio (defined as the quotient of the NOEC and predicted long-term environmental concentration);

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- (iv) where relevant, the bioconcentration and persistence of residues in earthworms.

2.5.2.6. Member States shall, where the evaluation carried out under point 2.5.1.1 does not exclude the possibility of the plant protection product reaching the soil under the proposed conditions of use, evaluate the impact on microbial activity such as the impact on nitrogen and carbon mineralisation processes in the soil after use of the plant protection product in accordance with the proposed conditions of use.

This evaluation shall take into consideration the following information:

- (i) all relevant information on the active substance, including the specific information relating to the effects of non-target soil micro-organisms as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;
- (ii) all relevant information on the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011, including the effects on non-target soil micro-organisms;
- (iii) where relevant, other authorised uses of plant protection products in the area of proposed use, containing the same active substance or which give rise to the same residues;
- (iv) all available information from biological primary screening.

## 2.6. *Analytical methods*

Member States shall evaluate the analytical methods proposed for post-registration control and monitoring purposes, to determine:

### 2.6.1. for formulation analysis:

the nature and quantity of the active substance(s) in the plant protection product and, where appropriate, any toxicologically, ecotoxicologically or environmentally significant impurities and co-formulants.

This evaluation shall take into consideration the following information:

- (i) the data on analytical methods as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;
- (ii) the data on analytical methods as provided for in the Annex to Regulation (EU) No 545/2011 and in particular:
  - the specificity and linearity of the proposed methods,
  - the importance of interferences,
  - the precision of the proposed methods (intralaboratory repeatability and interlaboratory reproducibility);
- (iii) the limit of detection and determination of the proposed methods for impurities.

### 2.6.2. for residue analysis:

the residues of the active substance, metabolites, breakdown or reaction products resulting from authorised uses of the plant protection product and which are of toxicological, ecotoxicological or environmental significance.

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This evaluation shall take into consideration the following information:

- (i) the data on analytical methods as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;
- (ii) the data on analytical methods as provided for in the Annex to Regulation (EU) No 545/2011 and in particular:
  - the specificity of the proposed methods,
  - the precision of the proposed methods (intralaboratory repeatability and interlaboratory reproducibility),
  - the recovery rate of the proposed methods at appropriate concentrations;
- (iii) the limit of detection of the proposed methods;
- (iv) the limit of determination of the proposed methods.

2.7. *Physical and chemical properties*

- 2.7.1. Member States shall evaluate the actual active substance content of the plant protection product and its stability during storage.
- 2.7.2. Member States shall evaluate the physical and chemical properties of the plant protection product and in particular:
  - where a suitable FAO (Food and Agriculture Organisation of the United Nations) specification exists, the physical and chemical properties addressed in that specification,
  - where no suitable FAO specification exists, all the relevant physical and chemical properties for the formulation as referred to in the 'Manual on the development and use of FAO and WHO specifications for plant protection products'.

This evaluation shall take into consideration the following information:

- (i) the data on the physical and chemical properties of the active substance as provided for in the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof;
  - (ii) the data on the physical and chemical properties of the plant protection product as provided for in the Annex to Regulation (EU) No 545/2011.
- 2.7.3. Where proposed label claims include requirements or recommendations for use of the plant protection product with other plant protection products or adjuvants as a tank mix, the physical and chemical compatibility of the products in the mixture must be evaluated.

C. **DECISION-MAKING**

1. **General principles**

- 1.1. Where appropriate, Member States shall impose conditions or restrictions with the authorisations they grant. The nature and severity of these measures must be selected on the basis of, and be appropriate to, the nature and extent of the expected advantages and the risks likely to arise.
- 1.2. Member States shall ensure that, where necessary, decisions taken with respect to the granting of authorisations take account of the agricultural, plant health or environmental (including climatic) conditions in the areas of envisaged use. Such considerations may result in specific conditions and restrictions of use, and, where necessary, in authorisation being granted for some but not other areas within the Member State in question.

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- 1.3. Member States shall ensure that the authorised amounts, in terms of rates and number of applications, are the minimum necessary to achieve the desired effect even where higher amounts would not result in unacceptable risks to human or animal health or to the environment. The authorised amounts must be differentiated in accordance with, and be appropriate to, the agricultural, plant health or environmental (including climatic) conditions in the various areas for which an authorisation is granted. However, the rates and the number of applications may not give rise to undesirable effects such as the development of resistance.
- 1.4. Member States shall ensure that decisions respect the principles of integrated control if the product is intended to be used in conditions where these principles are relied on.
- 1.5. Since the evaluation is to be based on data concerning a limited number of representative species, Member States shall ensure that use of plant protection products does not have any long-term repercussions for the abundance and diversity of non-target species.
- 1.6. Before issuing an authorisation, Member States shall ensure that the label of the product:
- fulfils the requirements setting out in the Commission Regulation (EU) 547/2011 <sup>(1)</sup>,
  - also contains the information on protection of users required by EU legislation on worker protection,
  - specifies in particular the conditions or restrictions under which the plant protection product may or may not be used as referred to in points 1.1, 1.2, 1.3, 1.4 and 1.5 above.
- The authorisation shall mention the particulars indicated in Directive 1999/45/EC of the European Parliament and of the Council <sup>(2)</sup> and in Regulation (EU) No 547/2011.
- 1.7. Before issuing authorisations, Member States shall:
- (a) ensure that the proposed packaging is in accordance with the provisions of Directive 1999/45/EC;
  - (b) ensure that:
    - the procedures for destruction of the plant protection product,
    - the procedures for neutralisation of the adverse effects of the product if it is accidentally dispersed, and
    - the procedures for the decontamination and destruction of the packaging,
 are in accordance with the relevant regulatory provisions.
- 1.8. No authorisation shall be granted unless all the requirements referred to in Section 2 are satisfied. However:
- (a) when one or more of the specific decision-making requirements referred to in points 2.1, 2.2, 2.3 or 2.7 are not fully satisfied, authorisations shall be granted only where the advantages of the use of the plant protection product under the proposed conditions of use outweigh the possible adverse effects of its use. Any restrictions on use of the product relating to non-compliance with some of the aforementioned requirements must be mentioned on the label, and non-compliance with the requirements referred to in point 2.7 must not compromise proper use of the product. These advantages can be in terms of:
    - advantages for and compatibility with integrated control measures or organic farming,
    - facilitating strategies to minimise the risk of development of resistance,

<sup>(1)</sup> See page 176 of this Official Journal.

<sup>(2)</sup> OJ L 200, 30.7.1999, p. 1.

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- the need for a greater diversity of types of active substances or biochemical modes of action, e.g. for use in strategies to avoid accelerated breakdown in the soil,
  - reduced risk for operators and consumers,
  - reduced contamination of the environment and reduced impact on non-target species;
- (b) where the criteria referred to in point 2.6 are not fully satisfied because of limitations in current analytical science and technology, authorisation shall be granted for a limited period if the methods submitted prove adequate for the purposes intended. In this case the applicant shall be given a time limit in which to develop and submit analytical methods that are in accordance with those criteria. The authorisation shall be reviewed on expiry of the time limit accorded to the applicant;
- (c) where the reproducibility of the submitted analytical methods referred to in point 2.6 has only been verified in two laboratories, an authorisation shall be granted for 1 year to permit the applicant to demonstrate the reproducibility of those methods in accordance with agreed criteria.

1.9. Where an authorisation has been granted in accordance with the requirements provided for in this Annex, Member States may, by virtue of Article 44 of Regulation (EC) No 1107/2009:

- (a) define, where possible, preferably in close cooperation with the applicant, measures to improve the performance of the plant protection product; and/or
- (b) define, where possible, in close cooperation with the applicant, measures to reduce further the exposure that could occur during and after use of the plant protection product.

Member States shall inform applicants of any measures identified under (a) or (b) and shall invite applicants to provide any supplementary data and information necessary to demonstrate performance or potential risks arising under the changed conditions.

## 2. **Specific principles**

The specific principles shall apply without prejudice to the general principles referred to in Section 1.

### 2.1. *Efficacy*

2.1.1. Where the proposed uses include recommendations for the control of or protection against organisms which are not considered to be harmful on the basis of experience acquired or scientific evidence under normal agricultural, plant health and environmental (including climatic) conditions in the areas of proposed use or where the other intended effects are not considered to be beneficial under those conditions, no authorisation shall be granted for those uses.

2.1.2. The level, consistency and duration of control or protection or other intended effects must be similar to those resulting from the use of suitable reference products. If no suitable reference product exists, the plant protection product must be shown to give a defined benefit in terms of the level, consistency and duration of control or protection or other intended effects under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

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- 2.1.3. Where relevant, yield response when the product is used and reduction of loss in storage must be quantitatively and/or qualitatively similar to those resulting from the use of suitable reference products. If no suitable reference product exists, the plant protection product must be shown to give a consistent and defined quantitative and/or qualitative benefit in terms of yield response and reduction of loss in storage under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.
- 2.1.4. Conclusions as to the performance of the preparation must be valid for all areas of the Member State in which it is to be authorised, and must hold for all conditions under which its use is proposed, except where the proposed label specifies that the preparation is intended for use in certain specified circumstances (e.g. light infestations, particular soil types or particular growing conditions).
- 2.1.5. Where proposed label claims include requirements for use of the preparation with other specified plant protection products or adjuvants as a tank mix, the mixture must achieve the desired effect and comply with the principles referred to in points 2.1.1 to 2.1.4.

Where proposed label claims include recommendations for use of the preparation with specified plant protection products or adjuvants as a tank mix, Member States shall not accept the recommendations unless they are justified.

2.2. *Absence of unacceptable effects on plants or plant products*

- 2.2.1. There must be no relevant phytotoxic effects on treated plants or plant products except where the proposed label indicates appropriate limitations of use.
- 2.2.2. There must be no reduction of yield at harvest due to phytotoxic effects below that which could be obtained without the use of the plant protection product, unless this reduction is compensated for by other advantages such as an enhancement of the quality of the treated plants or plant products.
- 2.2.3. There must be no unacceptable adverse effects on the quality of treated plants or plant products, except in the case of adverse effects on processing where proposed label claims specify that the preparation must not be applied to crops to be used for processing purposes.
- 2.2.4. There must be no unacceptable adverse effects on treated plants or plant products used for propagation or reproduction, such as effects on viability, germination, sprouting, rooting and establishment, except where proposed label claims specify that the preparation should not be applied to plants or plant products to be used for propagation or reproduction.
- 2.2.5. There must be no unacceptable impact on succeeding crops, except where proposed label claims specify that particular crops, which would be affected, must not be grown following the treated crop.
- 2.2.6. There must be no unacceptable impact on adjacent crops, except where proposed label claims specify that the preparation should not be applied when particular sensitive adjacent crops are present.
- 2.2.7. Where proposed label claims include requirements for use of the preparation with other plant protection products or adjuvants, as a tank mix, the mixture must comply with the principles referred to in points 2.2.1 to 2.2.6.

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2.2.8. The proposed instructions for cleaning the application equipment must be both practical and effective so that they can be applied with ease so as to ensure the removal of residual traces of the plant protection product which could subsequently cause damage.

2.3. *Impact on vertebrates to be controlled*

An authorisation for a plant protection product intended to eliminate vertebrates shall be granted only when:

- death is synchronous with the extinction of consciousness, or
- death occurs immediately, or
- vital functions are reduced gradually without signs of obvious suffering.

For repellent products, the intended effect shall be obtained without unnecessary suffering and pain for the target animals.

2.4. *Impact on human or animal health*

2.4.1. *Impact on human or animal health arising from the plant protection product*

2.4.1.1. No authorisation shall be granted if the extent of operator exposure in handling and using the plant protection product under the proposed conditions of use, including dose and application method, exceeds the AOEL.

Moreover, the conditions of the authorisation shall be in compliance with the limit value established for the active substance and/or toxicologically relevant compound(s) of the product in accordance with Council Directive 98/24/EC<sup>(1)</sup> and in accordance with Directive 2004/37/EC of the European Parliament and of the Council<sup>(2)</sup>.

2.4.1.2. Where the proposed conditions of use require use of items of protective clothing and equipment, no authorisation shall be granted unless those items are effective and in accordance with the relevant EU provisions and are readily obtainable by the user and unless it is feasible to use them under the circumstances of use of the plant protection product, taking into account climatic conditions in particular.

2.4.1.3. Plant protection products which because of particular properties or if mishandled or misused could lead to a high degree of risk must be subject to particular restrictions such as restrictions on the size of packaging, formulation type, distribution, use or manner of use.

Moreover, those plant protection products may not be authorised for use by non-professional users which are classified as:

- (i) acute toxicity category 1 and 2 for any route of uptake, provided the ATE (acute toxicity estimate) of the product does not exceed 25 mg/kg bw for the oral route of uptake or 0,25 mg/l/4h for the inhalation of dust, mist or fume;
- (ii) STOT (single exposure), category 1 (oral), provided their classification is due to the presence of classified substances showing significant non-lethal toxic effects at guidance values below 25 mg/kg bw;

<sup>(1)</sup> OJ L 131, 5.5.1998, p. 11.

<sup>(2)</sup> OJ L 158, 30.4.2004, p. 50.

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- (iii) STOT (single exposure), category 1 (dermal), provided their classification is due to the presence of classified substances showing significant non-lethal toxic effects at guidance values below 50 mg/kg bw;
- (iv) STOT (single exposure), category 1 (inhalation of gas/vapour), provided their classification is due to the presence of classified substances showing significant non-lethal toxic effects at guidance values below 0,5 mg/l/4h;
- (v) STOT (single exposure), category 1 (inhalation of dust/mist/fume), provided their classification is due to the presence of classified substances showing significant non-lethal toxic effects at guidance values below 0,25 mg/l/4h.

2.4.1.4. Waiting and re-entry safety periods or other precautions must be such that the exposure of bystanders or workers exposed after the application of the plant protection product does not exceed the AOEL levels established for the active substance or toxicologically relevant compound(s) in the plant protection product nor any limit values established for those compounds in accordance with the EU provisions referred to in point 2.4.1.1.

2.4.1.5. Waiting and re-entry safety periods or other precautions must be established in such a way that no adverse impact on animals occurs.

2.4.1.6. Waiting and re-entry periods or other precautions to ensure that the AOEL levels and limit values are respected must be realistic; if necessary special precautionary measures must be prescribed.

#### 2.4.2. Impact on human or animal health arising from residues

2.4.2.1. Authorisations must ensure that residues occurring reflect the minimum quantities of the plant protection product necessary to achieve adequate control corresponding to good agricultural practice, applied in such a manner (including pre-harvest intervals or withholding periods or storage periods) that the residues at harvest, slaughter or after storage, as appropriate, are reduced to a minimum.

2.4.2.2. Where the new circumstances under which the plant protection product is to be used do not correspond to those under which a MRL (maximum residue limit) was established previously, Member States shall not grant an authorisation for the plant protection product unless the applicant can provide evidence that its recommended use shall not exceed the MRL established under Regulation (EC) No 396/2005 of the European Parliament and of the Council <sup>(1)</sup>.

2.4.2.3. Where a MRL exists Member States shall not grant an authorisation for the plant protection product unless the applicant can provide evidence that its recommended use shall not exceed that MRL, or unless a new MRL has been established under Regulation (EC) No 396/2005.

2.4.2.4. In the cases referred to in points 2.4.2.2, each application for an authorisation must be accompanied by a risk assessment taking into account worst-case potential exposure of consumers in the Member State concerned on the basis of good agricultural practice.

Taking into account all registered uses, the proposed use shall not be authorised if the best possible estimate of dietary exposure exceeds the ADI.

<sup>(1)</sup> OJ L 70, 16.3.2005, p. 1.

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2.4.2.5. Where the nature of residues is affected during processing, a separate risk assessment may need to be carried out under the conditions provided for in point 2.4.2.4.

2.4.2.6. Where the treated plants or plant products are intended to be fed to animals, residues occurring shall not have an adverse effect on animal health.

2.5. *Influence on the environment*

2.5.1. *Fate and distribution in the environment*

2.5.1.1. No authorisation shall be granted if the active substance and, where they are of significance from the toxicological, ecotoxicological or environmental point of view, metabolites and breakdown or reaction products, after use of the plant protection product under the proposed conditions of use:

- during tests in the field, persist in soil for more than 1 year (i.e. DT90 > 1 year and DT50 > 3 months), or
- during laboratory tests, form non-extractable residues in amounts exceeding 70 % of the initial dose after 100 days with a mineralisation rate of less than 5 % in 100 days,

unless it is scientifically demonstrated that under field conditions there is no accumulation in soil at such levels that unacceptable residues in succeeding crops occur and/or that unacceptable phytotoxic effects on succeeding crops occur and/or that there is an unacceptable impact on the environment, in accordance with the relevant requirements provided for in points 2.5.1.2, 2.5.1.3, 2.5.1.4 and 2.5.2.

2.5.1.2. No authorisation shall be granted if the concentration of the active substance or of relevant metabolites, degradation or reaction products in groundwater, may be expected to exceed, as a result of use of the plant protection product under the proposed conditions of use, the lower of the following limit values:

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(i) the maximum permissible concentration laid down by Council Directive 98/83/EC <sup>(1)</sup>; or

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(ii) the maximum concentration laid down when approving the active substance in accordance with Regulation (EC) No 1107/2009, on the basis of appropriate data, in particular toxicological data, or, where that concentration has not been laid down, the concentration corresponding to one tenth of the ADI laid down when the active substance was approved in accordance with Regulation (EC) No 1107/2009,

unless it is scientifically demonstrated that under relevant field conditions the lower concentration is not exceeded.

2.5.1.3. No authorisation shall be granted if the concentration of the active substance or of relevant metabolites, breakdown or reaction products to be expected after use of the plant protection product under the proposed conditions of use in surface water:

- exceeds, where the surface water in or from the area of envisaged use is intended for the abstraction of drinking water, concentrations above which compliance with drinking water quality established in accordance with Directive 2000/60/EC of the European Parliament and of the Council <sup>(2)</sup> is compromised, or
- has an impact deemed unacceptable on non-target species, including animals, in accordance with the relevant requirements provided for in point 2.5.2.

The proposed instructions for use of the plant protection product, including procedures for cleaning application equipment, must be such that the likelihood of accidental contamination of surface water is reduced to a minimum.

<sup>(1)</sup> Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption (OJ L 330, 5.12.1998, p. 32).

<sup>(2)</sup> OJ L 327, 22.12.2000, p. 1.

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2.5.1.4. No authorisation shall be granted if the airborne concentration of the active substance under the proposed conditions of use is such that either the AOEL or the limit values for operators, bystanders or workers as referred to in point 2.4.1 are exceeded.

2.5.2. Impact on non-target species

2.5.2.1. Where there is a possibility of birds and other non-target terrestrial vertebrates being exposed, no authorisation shall be granted if:

— the acute and short-term toxicity/exposure ratio for birds and other non-target terrestrial vertebrates is less than 10 on the basis of LD<sub>50</sub> or the long-term toxicity/exposure ratio is less than 5, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact occurs after use of the plant protection product in accordance with the proposed conditions of use,

— the bioconcentration factor (BCF, related to fat tissue) is greater than 1, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable effects occur — directly or indirectly — after use of the plant protection product in accordance with the proposed conditions of use.

2.5.2.2. Where there is a possibility of aquatic organisms being exposed, no authorisation shall be granted if:

— the toxicity/exposure ratio for fish and Daphnia is less than 100 for acute exposure and less than 10 for long-term exposure, or

— the algal growth inhibition/exposure ratio is less than 10, or

— the maximum bioconcentration factor (BCF) is greater than 1 000 for plant protection products containing active substances which are readily biodegradable or greater than 100 for those which are not readily biodegradable,

unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact on the viability of exposed species (predators) occurs — directly or indirectly — after use of the plant protection product in accordance with the proposed conditions of use.

2.5.2.3. Where there is a possibility of honeybees being exposed, no authorisation shall be granted if the hazard quotients for oral or contact exposure of honeybees are greater than 50, unless it is clearly established through an appropriate risk assessment that under field conditions there are no unacceptable effects on honeybee larvae, honeybee behaviour, or colony survival and development after use of the plant protection product in accordance with the proposed conditions of use.

2.5.2.4. Where there is a possibility of beneficial arthropods other than honeybees being exposed, no authorisation shall be granted if more than 30 % of the test organisms are affected in lethal or sublethal laboratory tests conducted at the maximum proposed application rate, unless it is clearly established through an appropriate risk assessment that under field conditions there is no unacceptable impact on those organisms after use of the plant protection product in accordance with the proposed conditions of use. Any claims for selectivity and proposals for use in integrated pest management systems shall be substantiated by appropriate data.

2.5.2.5. Where there is a possibility of earthworms being exposed, no authorisation shall be granted if the acute toxicity/exposure ratio for earthworms is less than 10 or the long-term toxicity/exposure ratio is less than 5, unless it is clearly established through an appropriate risk assessment

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that under field conditions earthworm populations are not at risk after use of the plant protection product in accordance with the proposed conditions of use.

- 2.5.2.6. Where there is a possibility of non-target soil micro-organisms being exposed, no authorisation shall be granted if the nitrogen or carbon mineralisation processes in laboratory studies are affected by more than 25 % after 100 days, unless it is clearly established through an appropriate risk assessment that under field conditions there is no unacceptable impact on microbial activity after use of the plant protection product in accordance with the proposed conditions of use, taking account of the ability of micro-organisms to multiply.

2.6. *Analytical methods*

The methods proposed must reflect the state of the article. The following criteria must be met in order to permit validation of the analytical methods proposed for post-registration control and monitoring purposes:

2.6.1. for formulation analysis:

the method must be able to determine and to identify the active substance(s) and where appropriate any toxicologically, ecotoxicologically or environmentally significant impurities and co-formulants;

2.6.2. for residue analysis:

- (i) the method must be able to determine and confirm residues of toxicological, ecotoxicological or environmental significance;
- (ii) the mean recovery rates should be between 70 % and 110 % with a relative standard deviation of  $\leq 20$  %;
- (iii) the repeatability must be less than the following values for residues in foodstuffs:

| Residue level<br>mg/kg | Difference<br>mg/kg | Difference<br>in % |
|------------------------|---------------------|--------------------|
| 0,01                   | 0,005               | 50                 |
| 0,1                    | 0,025               | 25                 |
| 1                      | 0,125               | 12,5               |
| > 1                    |                     | 12,5               |

Intermediate values shall be determined by interpolation from a log-log graph;

- (iv) the reproducibility must be less than the following values for residues in foodstuffs:

| Residue level<br>mg/kg | Difference<br>mg/kg | Difference<br>in % |
|------------------------|---------------------|--------------------|
| 0,01                   | 0,01                | 100                |
| 0,1                    | 0,05                | 50                 |
| 1                      | 0,25                | 25                 |
| > 1                    |                     | 25                 |

Intermediate values are determined by interpolation from a log-log graph;

- (v) in the case of residue analysis in treated plants, plant products, foodstuffs, feedingstuffs or products of animal origin, except where the MRL or the proposed MRL is at the limit of determination, the sensitivity of the methods proposed must satisfy the following criteria:

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Limit of determination in relation to the proposed provisional or EU MRL:

| MRL<br>(mg/kg) | limit of determination<br>(mg/kg) |
|----------------|-----------------------------------|
| > 0,5          | 0,1                               |
| 0,5 – 0,05     | 0,1 – 0,02                        |
| < 0,05         | LMR × 0,5                         |

2.7. *Physical and chemical properties*

2.7.1. Where an appropriate FAO specification exists, that specification must be met.

2.7.2. Where no appropriate FAO specification exists, the physical and chemical properties of the product must meet the following requirements

(a) Chemical properties:

Throughout the shelf-life period, the difference between the stated and the actual content of the active substance in the plant protection product must not exceed the following values:

| Declared content in g/kg or g/l at<br>20 °C | Tolerance                          |
|---|------------------------------------|
| up to 25                                    | ± 15 % homogeneous formulation     |
|   | ± 25 % non-homogeneous formulation |
| more than 25 up to 100                      | ± 10 %                             |
| more than 100 up to 250                     | ± 6 %                              |
| more than 250 up to 500                     | ± 5 %                              |
| more than 500                               | ± 25 g/kg or ± 25 g/l              |

(b) Physical properties:

The plant protection product must fulfil the physical criteria (including storage stability) specified for the relevant formulation type in the 'Manual on the development and use of FAO and WHO specifications for plant protection products'.

2.7.3. Where the proposed label claims include requirements or recommendations for use of the preparation with other plant protection products or adjuvants as a tank mix and/or where the proposed label includes indications on the compatibility of the preparation with other plant protection products as a tank mix, those products or adjuvants must be physically and chemically compatible in the tank mix.

PART II

**Uniform principles for evaluation and authorisation of plant protection products containing micro-organisms**

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## A. INTRODUCTION

1. The principles developed in Part II aim to ensure that evaluations and decisions with regard to authorisation of plant protection products, provided they are microbial plant protection products, result in the implementation of the requirements of Article 29(1)(e) in conjunction with Article 4(3) and Article 29(f), (g) and (h) of Regulation (EC) No 1107/2009 by all Member States at a high level of protection of human and animal health and the environment.
2. In evaluating applications for granting authorisations Member States shall:
  - (a) — ensure that dossiers on microbial plant protection products supplied are in accordance with the requirements of part B of the Annex to Regulation (EU) No 545/2011, at the latest at the time of finalisation of the evaluation for the purpose of decision-making, without prejudice, where relevant, to Articles 33, 34 and 59 of Regulation (EC) No 1107/2009,
    - ensure that the data submitted are acceptable in terms of quantity, quality, consistency and reliability and sufficient to permit a proper evaluation of the dossier,
    - evaluate, where relevant, justifications submitted by the applicant for not supplying certain data;
  - (b) take into account the data referred to in part B of the Annex to Regulation (EU) No 544/2011, concerning the active substance consisting of micro-organisms (including viruses) in the plant protection product, submitted for the purpose of approval of the micro-organism concerned as active substances under Regulation (EC) No 1107/2009, and the results of the evaluation of those data, without prejudice, where relevant, to Article 33(3) and Articles 34 and 59 of Regulation (EC) No 1107/2009;
  - (c) take into consideration other relevant technical or scientific information they can reasonably possess with regard to the performance of the plant protection product or to the potentially adverse effects of the plant protection product, its components or its metabolites/toxins.
3. Where, in the specific principles on evaluation, reference is made to the data of part B of the Annex to Regulation (EU) No 544/2011 this shall be understood as being the data referred to in point 2(b).
4. Where the data and information provided are sufficient to permit completion of the evaluation for one of the proposed uses, applications must be evaluated and a decision made for the proposed use.

Taking account of justifications provided and with the benefit of any subsequent clarifications, Member States shall reject applications for granting authorisations for which the data gaps are such that it is not possible to finalise the evaluation and to make a reliable decision for at least one of the proposed uses.

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5. During the process of evaluation and decision-making, the Member State shall cooperate with the applicants in order to resolve any questions on the dossier quickly or to identify at an early stage any additional studies necessary for a proper evaluation of the dossier, or to amend any proposed conditions for the use of the plant protection product or to modify its nature or its composition in order to ensure full satisfaction of the requirements of this Annex or of Regulation (EC) No 1107/2009.

Member States shall normally come to a reasoned decision within 12 months of receiving a technically complete dossier. A technically complete dossier is one that satisfies all the requirements of part B of the Annex to Regulation (EU) No 545/2011.

6. The judgements made by the competent authorities of the Member States during the evaluation and decision-making process must be based on scientific principles, preferably recognised at international level, and be made with the benefit of expert advice.
7. A microbial plant protection product may contain viable and non-viable micro-organisms (including viruses) and formulation substances. It may also contain relevant metabolites/toxins produced during growth, residues from the growth medium, and microbial contaminants. The micro-organism, relevant metabolites/toxins and the plant protection product with residual growth medium and microbial contaminants present must all be evaluated.
8. Member States must take into account those guidance documents taken note of in the Standing Committee on the Food Chain and Animal Health (SCFCAH).
9. For genetically modified micro-organisms, Directive 2001/18/EC of the European Parliament and of the Council <sup>(1)</sup>, must be taken into account. The evaluation completed in the framework of that Directive must be provided and taken into account.
10. **Definitions and explanations of microbiological terms**

**Antibiosis:** A relationship between two or more species in which one species is actively harmed (as by the production of toxins by the harming species).

**Antigenic:** Any substance that, as a result of coming in contact with appropriate cells, induces a state of sensitivity and/or immune responsiveness after a latent period (days to weeks) and which reacts in a demonstrable way with antibodies and/or immune cells of the sensitised subject in vivo or in vitro.

**Antimicrobial:** Antimicrobial agents or antimicrobial(s) refer to naturally occurring, semi-synthetic or synthetic substances that exhibit antimicrobial activity (kill or inhibit the growth of micro-organisms).

The term antimicrobial(s) includes:

- antibiotics, which refer to substances produced by or derived from micro-organisms, and
- anticoccidials, which refer to substances that are active against coccidia, single cell protozoan parasites.

**CFU:** Colony-forming unit; one or more cells that grow to form a single visible colony.

**Colonisation:** Proliferation and persistence of a micro-organism in an environment, such as on external (skin) or internal body surfaces (intestine, lungs). For colonisation, the micro-organism must at least persist for a longer period than expected in a specific organ. The population of micro-organisms may decline but at a slower rate than normal

<sup>(1)</sup> OJ L 106, 17.4.2001, p. 1.

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clearance; it may be a steady population or it may be a growing population. Colonisation can be related to harmless and functional micro-organisms as well as to pathogenic micro-organisms. The possible occurrence of effects is not indicated.

Ecological niche: Unique environmental position occupied by a particular species, perceived in terms of actual physical space occupied and function performed within the community or ecosystem.

Host: An animal (including humans) or plant that harbours or nourishes another organism (parasite).

Host specificity: The range of different host-species that can be colonised by a microbial species or strain. A host-specific micro-organism colonises or has adverse effects on one or only a small number of different host-species. A non-host-specific micro-organism might colonise or might have adverse effects on a broad range of different host-species.

Infection: The introduction or entry of a pathogenic micro-organism into a susceptible host, whether or not it causes pathological effects or disease. The organism must enter the body of the host, usually the cells, and be able to reproduce to form new infective units. Simply ingesting a pathogen does not imply infection.

Infective: Capable of transmitting an infection.

Infectivity: The characteristics of a micro-organism that allow it to infect a susceptible host.

Invasion: The entry of a micro-organism into the host body (e.g. actual penetration of the integument, gut epithelial cells, etc.). 'Primary invasiveness' is a property of pathogenic micro-organisms.

Multiplication: Ability of a micro-organism to reproduce and increase in numbers during an infection.

Mycotoxin: A fungal toxin.

Non-viable micro-organism: A micro-organism that is not capable of replication or of transferring genetic material.

Non-viable residue: A residue that is not capable of replication or of transferring genetic material.

Pathogenicity: The ability of a micro-organism to cause disease and/or inflict damage on the host. Many pathogens cause disease by a combination of (i) toxicity and invasiveness or (ii) toxicity and colonising ability. However, some invasive pathogens cause disease that results from an abnormal reaction of the host's defence system.

Symbiosis: A type of interaction between organisms where one organism lives in intimate association with another, which is favourable for both organisms.

Viable micro-organism: A micro-organism that is capable of replication or of transferring genetic material.

Viable residue: A residue that is capable of replication or of transferring genetic material.

Viroid: Any of a class of infectious agents consisting of a small strand of RNA not associated with any protein. The RNA does not code for proteins and is not translated; it is replicated by host cell enzymes. Viroids are known to cause several plant diseases.

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Virulence: Measurement of the degree of disease producing ability of a micro-organism as indicated by the severity of the disease produced. Measure of the dosage (inoculum size) required to cause a specific degree of pathogenicity. It is measured experimentally by the median lethal dose (LD<sub>50</sub>) or median infective dose (ID<sub>50</sub>).

**B. EVALUATION**

The objective of an evaluation is to identify and assess, on a scientific basis and until further experience is reached on a case-by-case basis, potential adverse effects on human and animal health and the environment of the use of a microbial plant protection product. The evaluation shall also be carried out in order to identify the need for risk management measures and to identify and recommend suitable measures.

Due to the ability of micro-organisms to replicate, there is a clear difference between chemicals and micro-organisms used as plant protection products. Hazards arising are not necessarily of the same nature as those presented by chemicals, especially in relation to the capacity of micro-organisms to persist and multiply in different environments. Moreover, micro-organisms consist of a wide range of different organisms, all with their own unique characteristics. These differences between micro-organisms must be taken into account in the evaluation.

The micro-organism in the plant protection product should ideally function as a cell factory working directly on the spot where the target organism is harmful. Thus understanding the mode of action is a crucial step in the evaluation process.

Micro-organisms may produce a range of different metabolites (e.g. bacterial toxins or mycotoxins) many of which may have toxicological significance, and one or more of which may be involved in the mode of action of the plant protection product. The characterisation and identification of relevant metabolites must be assessed and the toxicity of these metabolites must be addressed. Information on production and/or relevance of metabolites may be deduced from:

- (a) toxicity studies;
- (b) biological properties of the micro-organism;
- (c) relationship to known plant, animal or human pathogens;
- (d) mode of action;
- (e) analytical methods.

On the basis of this information, metabolites may be considered as possibly being relevant. Therefore potential exposure to these metabolites must be assessed, in order to decide on their relevance.

**1. General principles**

1.1. Having regard to current scientific and technical knowledge, Member States shall evaluate the information provided in accordance with the requirements of part B of the Annex to Regulation (EU) No 544/2011 and part B of the Annex to Regulation (EU) No 545/2011 and in particular:

- (a) identify the hazards arising, assess their significance and make a judgement as to the likely risks to humans, animals or the environment; and
- (b) assess the performance in terms of efficacy and phytotoxicity/pathogenicity of the plant protection product for each use for which authorisation is sought.

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- 1.2. The quality/methodology of tests, where there are no standardised test methods, must be evaluated and the following characteristics, when available, of the methods described must be assessed:

relevance; representativeness; sensitivity; specificity; reproducibility; interlaboratory validations; predictiveness.

- 1.3. In interpreting the results of evaluations, Member States shall take into consideration possible elements of uncertainty in the information obtained during the evaluation, in order to ensure that the chances of failing to detect adverse effects or of underestimating their importance are reduced to a minimum. The decision-making process shall be examined to identify critical decision points or items of data for which uncertainties could lead to a false classification of risk.

The first evaluation made shall be based on the best available data or estimates reflecting the realistic conditions of use of the plant protection product. This shall be followed by a repeat evaluation, taking account of potential uncertainties in the critical data and of a range of use conditions that are likely to occur and resulting in a realistic worst-case approach, to determine whether it is possible that the initial evaluation could have been significantly different.

- 1.4. Member States shall evaluate each microbial plant protection product for which an application for authorisation is made in that Member State — the information evaluated for the micro-organism can be taken into account. Member States shall take into account the fact that any co-formulants might have an impact on the characteristics of the plant protection product compared to the micro-organism.

- 1.5. In evaluating applications and granting authorisations Member States shall consider the proposed practical conditions of use and in particular the purpose of use, the dose, the manner, frequency and timing of applications, and the nature and composition of the plant protection product. Whenever possible, Member States shall also take into account the principles of integrated pest control.

- 1.6. In the evaluation, Member States shall consider the agricultural, plant health or environmental (including climatic) conditions in the areas of use.

- 1.7. Where specific principles in Section 2 provide for the use of calculation models in the evaluation of a plant protection product, those models shall:

(a) make a best possible estimation of all relevant processes involved taking into account realistic parameters and assumptions;

(b) be submitted to an evaluation as referred to in point 1.3;

(c) be reliably validated with measurements carried out under circumstances relevant for the use of the model;

(d) be relevant to the conditions in the area of use;

(e) be supported with details indicating how the model calculates estimates provided, and explanations of all the inputs to the model and details of how they have been derived.

- 1.8. The data requirements, specified in part B of the Annex to Regulation (EU) No 544/2011 and part B of the Annex to Regulation (EU) No 545/2011, contain guidance as to when and how certain information must be submitted and as to procedures that must be followed when preparing and evaluating a dossier. That guidance must be respected.

**▼B****2. Specific principles**

Member States shall implement the following principles in the evaluation of the data and information submitted in support of applications, without prejudice to the general principles prescribed in Section 1:

**2.1. Identity****2.1.1. Identity of the micro-organism in the plant protection product**

The identity of the micro-organism shall be clearly established. It shall be ensured that the appropriate data are provided to allow for checking the identity of the micro-organism at strain level in the plant protection product.

The identity of the micro-organism shall be evaluated on the strain level. Where the micro-organism is either a mutant or a genetically modified organism<sup>(1)</sup>, the specific differences from other strains within the same species shall be recorded. Occurrence of resting stages shall be recorded.

The deposition of the strain at an internationally recognised culture collection shall be checked.

**2.1.2. Identity of the plant protection product**

Member States shall evaluate the detailed quantitative and qualitative information provided on the composition of the plant protection product, such as that concerning the micro-organism (see above), relevant metabolites/toxins, residual growth medium, co-formulants and microbial contaminants present.

**2.2. Biological, physical, chemical, and technical properties****2.2.1. Biological properties of the micro-organism in the plant protection product**

2.2.1.1. The origin of the strain, where relevant, its natural habitat including indications on the natural background level, life cycle and the possibilities for survival, colonisation, reproduction and dispersal must be evaluated. Proliferation of indigenous micro-organisms should after a short growth period level off and continue as for the background micro-organisms.

2.2.1.2. The ability of micro-organisms to adapt to the environment must be evaluated. In particular, Member States must take account of the following principles:

- (a) depending on the conditions (e.g. availability of substrates for growth and metabolism) micro-organisms can switch on or off the expression of given phenotypic traits;
- (b) the microbial strains most adapted to the environment can survive and multiply better than the non-adapted strains. Adapted strains have a selective advantage and can form the majority within a population after a number of generations;
- (c) the relatively rapid multiplication of micro-organisms leads to a higher frequency of mutations. If a mutation is promoting survival in the environment, the mutant strain can become dominant;
- (d) the properties of viruses, in particular, can change rapidly, including their virulence.

Therefore, where appropriate, information on the genetic stability of the micro-organism under the environmental conditions of proposed use must be evaluated, as well as information on the micro-organism's capacity to transfer genetic material to other organisms and information on the stability of encoded traits.

<sup>(1)</sup> See definition of 'genetically modified' in Directive 2001/18/EC.

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2.2.1.3. The mode of action of the micro-organism shall be evaluated in as much detail as appropriate. The possible role of metabolites/toxins for the mode of action shall be evaluated and when identified, the minimal effective concentration for each active metabolite/toxin shall be established. Information on mode of action can be a very valuable tool in identifying potential risks. Aspects to be considered in the evaluation, are:

- (a) antibiosis;
- (b) induction of plant resistance;
- (c) interference with the virulence of a pathogenic target organism;
- (d) endophytic growth;
- (e) root colonisation;
- (f) competition of ecological niche (e.g. nutrients, habitats);
- (g) parasitisation;
- (h) invertebrate pathogenicity.

2.2.1.4. In order to evaluate possible effects on non-target organisms, information on the micro-organism's host specificity must be evaluated, taking into account the characteristics and properties described in (a) and (b).

- (a) The ability of a micro-organism to be pathogenic for non-target organisms (humans, animals, and other non-target organisms) must be assessed. Any relationship to known plant, animal or human pathogens that are species of the genus of the active and/or contaminating micro-organisms must be assessed.
- (b) Pathogenicity as well as virulence is strongly related to the host-species (e.g. determined by body temperature, physiological environment) and to the host conditions (e.g. health condition, immune status). For example, multiplication in humans depends upon the ability of the micro-organism to grow at the body temperature of the host. Some micro-organisms can only grow and be metabolically active at temperatures far below or above human body temperature, and therefore can not be pathogenic for humans. However, the route of entry of the micro-organism into the host (oral, inhalation, skin/wound) can also be the critical factor. For example, a microbial species may cause a disease following entry via skin damage, but not via the oral route.

2.2.1.5. Many micro-organisms produce antibiosis substances that cause normal interferences in the microbial community. Resistance to antimicrobial agents of importance for human and veterinary medicine must be assessed. The possibility for transfer of genes that code for resistance to antimicrobial agents must be evaluated.

2.2.2. Physical, chemical and technical properties of the plant protection product

2.2.2.1. Depending on the nature of the micro-organism and the formulation type, the technical properties of the plant protection product must be evaluated.

2.2.2.2. Shelf-life and storage stability of the preparation must be evaluated, taking into account possible changes in composition such as growth of the micro-organism or of contaminating micro-organisms, production of metabolites/toxins, etc.

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2.2.2.3. Member States shall evaluate the physical and chemical properties of the plant protection product and the retention of these characteristics after storage and take into consideration:

- (a) where a suitable Food and Agriculture Organisation of the United Nations (FAO) specification exists, the physical and chemical properties addressed in that specification;
- (b) where no suitable FAO specification exists, all relevant physical and chemical properties for the formulation referred to in the Manual on the development and use of FAO and World Health Organisation (WHO) specifications for pesticides.

2.2.2.4. Where the proposed label claims include requirements or recommendations for use of the preparation with other plant protection products or adjuvants as a tank mix, and/or where the proposed label includes indications concerning the compatibility of the preparation with other plant protection products as a tank mix, those plant protection products or adjuvants must be physically and chemically compatible in the tank mix. Biological compatibility must also be demonstrated for tank-mixtures, i.e. it must be shown that each plant protection product in the mixture performs as expected and that no antagonism occurs.

2.3. *Further information*

2.3.1. **Quality control of the production of the micro-organism in the plant protection product**

The quality assurance criteria proposed for production of the micro-organism must be evaluated. In the evaluation criteria relating to process control, good manufacturing practice, operational practices, process flows, cleaning practices, microbial monitoring and hygiene conditions should be taken into account to ensure good quality of the micro-organism. The quality, stability, purity, etc., of the micro-organism must be addressed in the quality control system.

2.3.2. **Quality control of the plant protection product**

The quality assurance criteria proposed must be evaluated. If the plant protection product contains metabolites/toxins produced during growth and residues from the growth medium this should be evaluated. The possibility of the occurrence of contaminating micro-organisms must be evaluated.

2.4. *Efficacy*

2.4.1. Where the proposed use concerns the control of or protection against an organism, Member States shall evaluate the possibility that this organism could be harmful under the agricultural, plant health and environmental (including climatic) conditions in the area of the proposed use.

2.4.2. Member States shall evaluate whether significant damage, loss or inconvenience could occur under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use if the plant protection product were not used.

2.4.3. Member States shall evaluate the efficacy data provided for in part B of the Annex to Regulation (EU) No 545/2011 on the plant protection product having regard to the degree of control or the extent of the effect desired and having regard to relevant experimental conditions such as:

- (a) the choice of the crop or cultivar;

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- (b) the agricultural and environmental (including climatic) conditions (if necessary for acceptable efficacy such data/information should also be given for the time before and after application);
- (c) the presence and density of the harmful organism;
- (d) the development stage of crop and organism;
- (e) the amount of the microbial plant protection product used;
- (f) if required on the label, the amount of adjuvant added;
- (g) the frequency and timing of the applications;
- (h) the type of application equipment;
- (i) the need for any special cleaning measures for the application equipment.

2.4.4. Member States shall evaluate the performance of the plant protection product under the range of agricultural, plant health and environmental (including climatic) conditions likely to be encountered in practice in the area of proposed use. The effect on integrated control shall be included in the evaluation. In particular, consideration shall be paid to:

- (a) the level, consistency and duration of the effect sought in relation to the dose in comparison with a suitable reference product or products, where they exist, and an untreated control;
- (b) where relevant, the effect on yield or reduction of loss in storage, in terms of quantity and/or quality, in comparison with a suitable reference product or products, where they exist, and an untreated control.

Where no suitable reference product exists, Member States shall evaluate the performance of the plant protection product to determine whether there is a consistent and defined benefit under the agricultural, plant health and environmental (including climatic) conditions likely to be encountered in practice in the area of proposed use.

2.4.5. Member States shall evaluate the degree of adverse effects on the treated crop after use of the plant protection product in accordance with the proposed conditions of use in comparison, where relevant, with a suitable reference product or products, where they exist, and/or an untreated control.

- (a) This evaluation shall take into consideration the following information:
  - (i) efficacy data;
  - (ii) other relevant information on the plant protection product such as nature of the plant protection product, dose, method of application, number and timing of applications, incompatibility with other crop treatments;
  - (iii) all relevant information on the micro-organism, including biological properties e.g. mode of action, survival, host specificity.
- (b) This evaluation shall include:
  - (i) the nature, frequency, level and duration of observed phytotoxic/phytopathogenic effects and the agricultural, plant health and environmental (including climatic) conditions that affect them;

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- (ii) differences between main cultivars with regard to their sensitivity to phytotoxic/phytopathogenic effects;
- (iii) the part of the treated crop or plant products where phytotoxic/phytopathogenic effects are observed;
- (iv) adverse impact on the yield of the treated crop or plant products in terms of quantity and/or quality;
- (v) adverse impact on treated plants or plant products to be used for propagation, in terms of viability, germination, sprouting, rooting and establishment;
- (vi) where micro-organisms are disseminated, the adverse impact on adjacent crops.

- 2.4.6. Where the label of the plant protection product includes requirements for use of the plant protection product with other plant protection products and/or with adjuvants as a tank mix, Member States shall make the evaluations referred to in points 2.4.3 to 2.4.5 in relation to the information supplied for the tank mix.

Where the label of the plant protection product label includes recommendations for use of the plant protection product with other plant protection products and/or with adjuvants as a tank mix, Member States shall evaluate the appropriateness of the mix and of its conditions of use.

- 2.4.7. Where the available data indicate that the micro-organism or significant relevant metabolites/toxins, degradation and reaction products of the formulants persist in soils and/or in or on plant substances in significant quantities after use of the plant protection product in accordance with the proposed conditions of use, Member States shall evaluate the degree of adverse effects on subsequent crops.
- 2.4.8. Where the proposed use of a plant protection product is intended to have an effect on vertebrates, Member States shall evaluate the mechanism by which this effect is obtained and the observed effects on the behaviour and health of the target animals. When the intended effect is to kill the target animal they shall evaluate the time necessary to obtain the death of the animal and the conditions under which death occurs.

This evaluation shall take into consideration the following information:

- (a) all relevant information as provided for in part B of the annex to Regulation (EU) No 545/2011 and the results of the evaluation thereof, including the toxicological studies;
- (b) all relevant information on the plant protection product as provided for in part B of the Annex to Regulation (EU) No 545/2011, including toxicological studies and efficacy data.

2.5. *Identification/detection and quantification methods*

Member States shall evaluate the analytical methods proposed for post-registration control and monitoring purposes of the viable and non-viable components both in the formulation and as residues in or on treated crops. Sufficient validation is required for pre-authorisation methods and post-authorisation monitoring methods. Methods that are considered suitable for post-authorisation monitoring must be clearly identified.

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## 2.5.1. Analytical methods for the plant protection product

2.5.1.1. *Non-viable components*

Member States shall evaluate the analytical methods proposed to identify and quantify the toxicologically, ecotoxicologically or environmentally significant non-viable components resulting from the micro-organism and/or present as impurity or co-formulant (including eventually resulting breakdown and/or reaction products thereof).

This evaluation shall take into consideration the information on analytical methods provided for in part B of the Annex to Regulation (EU) No 544/2011 and in part B of the Annex to Regulation (EU) No 545/2011 and the results of the evaluation thereof. In particular, the following information must be taken into account:

- (a) the specificity and linearity of the proposed methods;
- (b) the precision (repeatability) of the proposed methods;
- (c) the importance of interferences;
- (d) the accuracy of the proposed methods at appropriate concentrations;
- (e) the limit of quantification of the proposed methods.

2.5.1.2. *Viable components*

Member States shall evaluate the methods proposed to quantify and identify the specific strain concerned and especially methods that discriminate that strain from closely related strains.

This evaluation shall take into consideration the information on analytical methods provided for in part B of the Annex to Regulation (EU) No 544/2011 and in part B of the Annex to Regulation (EU) No 545/2011 and the results of the evaluation thereof. In particular, the following information must be taken into account:

- (a) the specificity of the proposed methods;
- (b) the precision (repeatability) of the proposed methods;
- (c) the importance of interferences;
- (d) the quantifiability of the proposed methods.

## 2.5.2. Analytical methods for the determination of residues

2.5.2.1. *Non-viable residues*

Member States shall evaluate the analytical methods proposed to identify and quantify the toxicologically, ecotoxicologically or environmentally significant non-viable residues resulting from the micro-organism (including eventually resulting breakdown and/or reaction products thereof).

This evaluation shall take into consideration the information on analytical methods provided for in part B of the Annex to Regulation (EU) No 544/2011 and in part B of the Annex to Regulation (EU) No 545/2011 and the results of the evaluation thereof. In particular, the following information must be taken into account:

- (a) the specificity and linearity of the proposed methods;
- (b) the precision (repeatability) of the proposed methods;

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- (c) the reproducibility (independent laboratory validation) of the proposed methods;
- (d) the importance of interferences;
- (e) the accuracy of the proposed methods at appropriate concentrations;
- (f) the limit of quantification of the proposed methods.

2.5.2.2. *Viable residues*

Member States shall evaluate the methods proposed to identify the specific strain concerned and especially methods that discriminate that strain from closely related strains.

This evaluation shall take into consideration the information on analytical methods provided for in part B of the Annex to Regulation (EU) No 544/2011 and in part B of the Annex to Regulation (EU) No 545/2011 and the results of the evaluation thereof. In particular, the following information must be taken into account:

- (a) the specificity of the proposed methods;
- (b) the precision (repeatability) of the proposed methods;
- (c) the importance of interferences;
- (d) the quantifiability of the proposed methods.

2.6. *Impact on human or animal health*

The impact on human or animal health must be evaluated. In particular, Member States must take account of the following principles:

- (a) due to the ability of micro-organisms to replicate, there is a clear difference between chemicals and micro-organisms used as plant protection products. Hazards arising are not necessarily of the same nature as those presented by chemicals, especially in relation to the capacity of micro-organisms to persist and multiply in different environments;
- (b) the pathogenicity of the micro-organism to humans and non-target animals, the infectiveness of the micro-organism, the ability of the micro-organism to colonise, the toxicity of metabolites/toxins as well as the toxicity of the residual growth medium, contaminants and co-formulants, are important endpoints in assessing adverse effects arising from the plant protection product;
- (c) colonisation, infectiveness and toxicity comprise a complex set of interactions between micro-organisms and hosts and these endpoints may not be resolved easily as independent endpoints;
- (d) in combining these endpoints, the most important aspects of the micro-organism that must be assessed are:
  - ability to persist and multiply in a host (indicative of colonisation or infectivity),
  - ability to produce non-adverse or adverse effects in a host, indicative of infectivity, pathogenicity, and/or toxicity;

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- (e) moreover, the complexity of the biological issues shall be taken into account in evaluating the hazards and risks presented by use of these plant protection products for human and animals. An assessment of pathogenicity and infectiveness is necessary even if the potential of exposure is deemed low;
- (f) for risk assessment purposes the acute toxicity studies used shall, where available, include at least two doses (e.g. one very high dose and one corresponding to the expected exposure under practical conditions).

#### 2.6.1. Effects on human or animal health arising from the plant protection product

2.6.1.1. Member States shall evaluate operator exposure to the micro-organism, and/or to toxicologically relevant compounds in the plant protection product (e.g. their metabolites/toxins, residual growth medium, contaminants and co-formulants), likely to occur under the proposed conditions of use (including in particular dose, application method and climatic conditions). Realistic data on exposure levels must be used and, if such data are not available, a suitable, validated calculation model. When available, a European harmonised generic exposure database for plant protection products shall be used.

- (a) This evaluation shall take into consideration the following information:

- (i) the medical data and the toxicity, infectivity and pathogenicity studies as provided for in part B of the Annex to Regulation (EU) No 544/2011, and the results of the evaluation thereof. Tier 1 tests shall permit an evaluation to be made of a micro-organism with respect to its ability to persist or grow in the host and its ability to cause effects/reactions in the host. Parameters that indicate the absence of ability to persist and multiply in the host, and the absence of ability to produce non-adverse or adverse effects in a host, include fast and complete clearance from the body, no activation of the immune system, no histopathological changes, and for replication temperatures far below or far above mammalian body temperatures. These parameters can in some cases be assessed using acute studies and existing human data, and sometimes can only be assessed using repeated dose studies.

Evaluation based on relevant parameters of Tier 1 tests shall lead to an assessment of the possible effects of occupational exposure, taking into account the intensity and duration of exposure including exposure due to repeated use during practical use.

The toxicity of certain metabolites/toxins can only be assessed, if it has been demonstrated that the test animals are actually exposed to these metabolites/toxins;

- (ii) other relevant information on the micro-organism, the metabolites/toxins, residual growth medium, contaminants and co-formulants in the plant protection product, such as their biological, physical and chemical properties (e.g. survival of the micro-organism at the body temperature of humans and animals, ecological niche, behaviour of the micro-organism and/or metabolites/toxins during application);

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- (iii) the toxicological studies provided for in part B of the Annex to Regulation (EU) No 545/2011;
- (iv) other relevant information provided for in part B of the Annex to Regulation (EU) No 545/2011 such as:
  - composition of the preparation,
  - nature of the preparation,
  - size, design and type of packaging,
  - field of use and nature of the crop or target,
  - method of application including handling, loading and mixing of the plant protection product,
  - exposure reduction measures recommended,
  - protective clothing recommendations,
  - maximum application rate,
  - minimum spray application volume stated on the label,
  - number and timing of applications.
- (b) On the basis of the information referred to in (a) the following overall end-points should be established for single or repeated operator exposure following the intended use:
  - persistence or growth of the micro-organism in the host,
  - adverse effects observed,
  - observed or expected effects of contaminants (including contaminating micro-organisms),
  - observed or expected effects of relevant metabolites/toxins.

If there are indications of colonisation in the host and/or if any adverse effects, indicative of toxicity/infectivity are observed, taking into account the exposure scenario (i.e. acute or repeated exposure), further testing is indicated.

- (c) This evaluation shall be made for each type of application method and application equipment proposed for use of the plant protection product as well as for the different types and sizes of containers to be used, taking into account mixing, loading operations, application of the plant protection product and cleaning and routine maintenance of application equipment. Where relevant, other authorised uses of the plant protection product in the area of envisaged use containing the same active substance or which give rise to the same residues may also be taken into account. It shall be taken into account that if replication of the micro-organism is expected, exposure assessment could be highly speculative.
- (d) The absence or presence of the potential for colonisation or the possibility of effects in operators at the tested dose levels as provided for in part B of the Annex to Regulation (EU) No 544/2011 and in part B of the Annex to Regulation (EU) No 545/2011 shall be assessed with regard to measured or estimated levels of human exposure. This risk assessment, preferably quantitative, shall include consideration of e.g. mode of action, biological, physical and chemical properties of the micro-organism and other substances in the formulation.

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2.6.1.2. Member States shall examine information relating to the nature and characteristics of the packaging proposed with particular reference to the following aspects:

- (a) the type of packaging;
- (b) its dimensions and capacity;
- (c) the size of the opening;
- (d) the type of closure;
- (e) its strength, leakproofness and resistance to normal transport and handling;
- (f) its resistance to and compatibility with the contents.

2.6.1.3. Member States shall examine the nature and characteristics of the protective clothing and equipment proposed with particular reference to the following aspects:

- (a) obtainability and suitability;
- (b) effectiveness;
- (c) ease of wearing taking into account physical stress and climatic conditions;
- (d) resistance to and compatibility with the plant protection product.

2.6.1.4. Member States shall evaluate the possibility of exposure of other humans (workers exposed after the application of the plant protection product, such as re-entering workers, or bystanders) or animals to the micro-organism and/or to other toxicologically relevant compounds in the plant protection product under the proposed conditions of use. This evaluation shall take into consideration the following information:

- (a) the medical data and the toxicity, infectivity and pathogenicity studies provided for in part B of the Annex to Regulation (EU) No 544/2011, and the results of the evaluation thereof. Tier 1 tests shall permit an evaluation to be made of a micro-organism with respect to its ability to persist or grow in the host and its ability to cause effects/reactions in the host. Parameters that indicate the absence of ability to persist and multiply in the host, and the absence of ability to produce non-adverse or adverse effects in a host, include rapid and complete clearance from the body, no activation of the immune system, no histopathological changes, and inability to replicate at mammalian body temperatures. These parameters can in some cases be assessed using acute studies and existing human data, and sometimes can only be assessed using repeated dose studies.

Evaluation based on relevant parameters of Tier 1 tests shall lead to an assessment of the possible effects of occupational exposure, taking into account the intensity and duration of exposure, including exposure due to repeated use during practical use.

The toxicity of certain metabolites/toxins can only be assessed, if it has been demonstrated that the test animals are actually exposed to these metabolites/toxins;

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- (b) other relevant information on the micro-organism, the metabolites/toxins, residual growth medium, contaminants and co-formulants in the plant protection product, such as their biological, physical and chemical properties (e.g. survival of the micro-organism at the body temperature of humans and animals, ecological niche, behaviour of the micro-organism and/or metabolites/toxins during application);
- (c) the toxicological studies provided for in part B of the Annex to Regulation (EU) No 545/2011;
- (d) other relevant information on the plant protection product as provided for in part B of the Annex to Regulation (EU) No 545/2011, such as:
  - re-entry periods, necessary waiting periods or other precautions to protect humans and animals,
  - method of application, in particular spraying,
  - maximum application rate,
  - minimum spray application volume,
  - composition of the preparation,
  - excess remaining on plants and plant products after treatment, taking into account the influence of factors such as temperature, UV light, pH and the presence of certain substances,
  - further activities whereby workers are exposed.

## 2.6.2. Effects on human or animal health arising from residues

In the evaluation, non-viable and viable residues must be addressed separately. Viruses and viroids should be considered as viable residues since they are capable of transferring genetic material, although strictly speaking they are not living.

### 2.6.2.1. *Non-viable residues*

- (a) Member States shall evaluate the possibility of exposure of humans or animals to non-viable residues and their degradation products via the food chain due to the possible occurrence of such residues in or on edible parts of treated crops. In particular, the following information should be taken into account:
  - the stage of development of the micro-organism at which non-viable residues are produced,
  - the development stages/life cycle of the micro-organism under typical environmental conditions; in particular, attention shall be paid to the assessment of the likelihood of survival and multiplication of the micro-organism in or on crops, food or feed, and, as a consequence, the likelihood of the production of non-viable residues,
  - the stability of relevant non-viable residues (including the effects of factors such as temperature, UV light, pH and the presence of certain substances),
  - any experimental study showing whether or not relevant non-viable residues are translocated in plants,

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- data concerning the proposed good agricultural practice (including number and timing of applications, maximum application rate and minimum spray application volume, proposed pre-harvest intervals for envisaged uses, or withholding periods or storage periods, in the case of post-harvest uses) and additional data on application as provided for in part B of the Annex to Regulation (EU) No 545/2011,
  - where relevant, other authorised uses of plant protection products in the area of envisaged use, i.e. containing the same residues, and
  - the natural occurrence of non-viable residues on edible plant parts as a consequence of naturally occurring micro-organisms.
- (b) Member States shall evaluate the toxicity of non-viable residues and their degradation products having regard in particular to the specific information provided in accordance with part B of the Annex to Regulation (EU) No 544/2011 and in part B of the Annex to Regulation (EU) No 545/2011.
- (c) Where non-viable residues or their degradation products are considered toxicologically relevant for humans and/or animals and when exposure is not considered negligible, the actual levels in or on the edible parts of treated crops shall be determined, taking into consideration:
- analytical methods for the non-viable residues,
  - the growth curves of the micro-organism under optimal conditions,
  - the production/formation of non-viable residues at relevant moments (e.g. at the anticipated harvest time).

*2.6.2.2. Viable residues*

- (a) Member States shall evaluate the possibility of exposure of humans or animals to viable residues via the food chain due to the possible occurrence of such residues in or on edible parts of treated crops. In particular, the following information should be taken into account:
- the likelihood of survival, the persistence and multiplication of the micro-organism in or on crops, food or feed. The various development stages/life cycle of the micro-organism shall be addressed,
  - information concerning its ecological niche,
  - information on fate and behaviour in the various parts of the environment,
  - the natural occurrence of the micro-organism (and/or a related micro-organism),
  - data concerning the proposed good agricultural practice (including number and timing of applications, maximum application rate and minimum spray application volume, proposed pre-harvest intervals for envisaged uses, or withholding periods or storage periods in the case of post-harvest uses) and additional data on application as provided for in part B of the Annex to Regulation (EU) No 545/2011,

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- where relevant, other authorised uses of plant protection products in the area of envisaged use, i.e. containing the same micro-organism or which result in the same residues.
- (b) Member States shall evaluate the specific information concerning the ability of viable residues to persist or grow in the host and the ability of such residues to cause effects/reactions in the host. In particular, the following information shall be taken into account:
- the medical data and toxicity, infectivity and pathogenicity studies provided for in part B of the Annex to Regulation (EU) No 544/2011 and the results of the evaluation thereof,
  - the development stages/life cycle of the micro-organism under typical environmental conditions (e.g. in or on the treated crop),
  - the mode of action of the micro-organism,
  - the biological properties of the micro-organism (e.g. host specificity).

The various development stages/life cycle of the micro-organism shall be addressed.

- (c) In the event that viable residues are considered to be toxicologically relevant for humans and/or animals and if exposure is not considered negligible, the actual levels in or on the edible parts of treated crops shall be determined, taking into consideration:
- analytical methods for the viable residues,
  - the growth curves of the micro-organism under optimal conditions,
  - the possibilities of extrapolating data from one crop to another.

#### 2.7. *Fate and behaviour in the environment*

The biocomplexity of the ecosystems and interactions in the microbial communities concerned must be taken into account.

Information on the origin and properties (e.g. specificity) of the micro-organism/its residual metabolites/toxins and its intended use forms the basis for an assessment of environmental fate and behaviour. The mode of action of the micro-organism shall be taken into consideration.

An assessment shall be made of the fate and behaviour of any known relevant metabolite that is produced by the micro-organism. The assessment shall be made for each environmental compartment, and shall be triggered on the basis of the criteria specified in section 7 (iv) of part B of the Annex to Regulation (EU) No 544/2011.

In the assessment of the environmental fate and behaviour of plant protection products, Member States shall have regard to all aspects of the environment, including biota. The potential for persistence and multiplication of micro-organisms has to be assessed in all environmental compartments unless it can be justified that particular micro-organisms shall not reach a specific compartment. The mobility of micro-organisms and their residual metabolites/toxins must be considered.

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- 2.7.1. Member States shall evaluate the possibility of contamination of ground water, surface water and drinking water under the proposed conditions of use of the plant protection product.

In the overall assessment, Member States shall pay particular attention to potential adverse effects on humans through groundwater contamination, when the active substance is applied in regions with vulnerable conditions, such as drinking water abstraction areas.

- 2.7.2. Member States shall evaluate the risk for the aquatic compartment where the possibility of the exposure of aquatic organisms has been established. A micro-organism may give rise to risks because of its potential through multiplication to establish itself in the environment and can therefore have a long-lasting or permanent impact on microbial communities or their predators.

This evaluation shall take into consideration the following information:

- (a) the biological properties of the micro-organism;
  - (b) the survival of the micro-organism in the environment;
  - (c) its ecological niche;
  - (d) the natural background level of the micro-organism, where it is indigenous;
  - (e) information on fate and behaviour in the various parts of the environment;
  - (f) where relevant, information on potential interference with analytical systems used for the control of the quality of drinking water as provided for in Council Directive 98/83/EC <sup>(1)</sup>;
  - (g) where relevant, other authorised uses of plant protection products in the area of envisaged use, e.g. containing the same active substance or which gives rise to the same residues.
- 2.7.3. Member States shall evaluate the possibility of exposure of organisms in the atmosphere to the plant protection product under the proposed conditions of use; if this possibility exists they shall evaluate the risk for the atmosphere. The transport, short-range and long-range, of the micro-organism in the atmosphere shall be taken into account.
- 2.7.4. Member States shall evaluate the possibility of exposure of organisms in the terrestrial compartment to the plant protection product under the proposed conditions of use; if this possibility exists they shall evaluate the risks arising for the terrestrial compartment. A micro-organism may give rise to risks because of its potential through multiplication to establish itself in the environment and can therefore have a long-lasting or permanent impact on microbial communities or their predators.

This evaluation shall take into consideration the following information:

- (a) the biological properties of the micro-organism;
- (b) the survival of the micro-organism in the environment;
- (c) its ecological niche;
- (d) the natural background level of the micro-organism, where it is indigenous;
- (e) information on fate and behaviour in the various parts of the environment;

<sup>(1)</sup> OJ L 330, 5.12.1998, p. 32.

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- (f) where relevant, other authorised uses of plant protection products in the area of envisaged use, e.g. containing the same active substance or which gives rise to the same residues.

#### 2.8. *Effects on and exposure of non-target organisms*

Information on the ecology of the micro-organism and effects on the environment shall be assessed as well as possible exposure levels and the effects of its relevant metabolites/toxins. An overall assessment of the environmental risks that the plant protection product may cause, taking into account the normal levels of exposure to micro-organisms both in the environment as well as in the body of organisms, is necessary.

Member States shall evaluate the possibility of exposure of non-target organisms under the proposed conditions of use and if this possibility exists they shall evaluate the risks arising for the non-target organisms concerned.

Where applicable, an assessment of infectivity and pathogenicity is necessary, unless it can be justified that non-target organisms shall not be exposed.

To assess the possibility of exposure the following information shall also be taken into consideration:

- (a) the survival of the micro-organism in the respective compartment;
- (b) its ecological niche;
- (c) the natural background level of the micro-organism, where it is indigenous;
- (d) information on fate and behaviour in the various parts of the environment;
- (e) where relevant, other authorised uses of the plant protection product in the area of envisaged use containing the same active substance or which give rise to the same residues.

#### 2.8.1. Member States shall evaluate the possibility of exposure of and effects on terrestrial wildlife (non-domestic birds, mammals and other terrestrial vertebrates).

##### 2.8.1.1. A micro-organism may give rise to risks because of its potential to infect and multiply in avian and mammalian host systems. Whether or not identified risks could be changed due to the formulation of the plant protection product shall be assessed, taking into account the following information on the micro-organism:

- (a) its mode of action;
- (b) other biological properties;
- (c) studies on mammalian toxicity, pathogenicity and infectivity;
- (d) studies on avian toxicity, pathogenicity and infectivity.

##### 2.8.1.2. A plant protection product may give rise to toxic effects due to the action of toxins or co-formulants. For the assessment of such effects, the following information shall be taken into consideration:

- (a) studies on mammalian toxicity;
- (b) studies on avian toxicity;

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- (c) information on fate and behaviour in the various parts of the environment.

If mortality or signs of intoxication are observed in the tests the evaluation must include a calculation of toxicity/exposure ratios based on the quotient of the LD<sub>50</sub> value and the estimated exposure expressed in mg/kg body weight.

- 2.8.2. Member States shall evaluate the possibility of exposure of and effects on aquatic organisms.

- 2.8.2.1. A micro-organism may give rise to risks because of its potential to infect and multiply in aquatic organisms. Whether or not identified risks could be changed due to the formulation of the plant protection product shall be assessed, taking into account the following information on the micro-organism:

- (a) its mode of action;
- (b) other biological properties;
- (c) studies on toxicity, pathogenicity and infectivity.

- 2.8.2.2. A plant protection product may give rise to toxic effects due to the action of toxins or co-formulants. For the assessment of such effects the following information shall be taken into consideration:

- (a) studies on toxicity to aquatic organisms;
- (b) information on fate and behaviour in the various parts of the environment.

If mortality or signs of intoxication are observed in the tests the evaluation must include a calculation of toxicity/exposure ratios based on the quotient of the EC<sub>50</sub> value and/or the NOEC value and the estimated exposure.

- 2.8.3. Member States shall evaluate the possibility of exposure of and effects on bees.

- 2.8.3.1. A micro-organism may give rise to risks because of its potential to infect and multiply in bees. Whether or not identified risks could be changed due to the formulation of the plant protection product shall be assessed, taking into account the following information on the micro-organism:

- (a) its mode of action;
- (b) other biological properties;
- (c) studies on toxicity, pathogenicity and infectivity.

- 2.8.3.2. A plant protection product may give rise to toxic effects due to the action of toxins or co-formulants. For the assessment of such effects the following information shall be taken into consideration:

- (a) studies on toxicity to bees;
- (b) information on fate and behaviour in the various parts of the environment.

If mortality or signs of intoxication are observed in the tests the evaluation must include a calculation of the hazard quotient, based on the quotient of the dose in g/ha and the LD<sub>50</sub> value in µg/bee.

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2.8.4. Member States shall evaluate the possibility of exposure of and effects on arthropods other than bees.

2.8.4.1. A micro-organism may give rise to risks because of its potential to infect and multiply in arthropods other than bees. Whether or not identified risks could be changed due to the formulation of the plant protection product shall be assessed, taking into account the following information on the micro-organism:

- (a) its mode of action;
- (b) other biological properties;
- (c) studies on toxicity, pathogenicity and infectivity to honeybees and other arthropods.

2.8.4.2. A plant protection product may give rise to toxic effects due to the action of toxins or co-formulants. For the assessment of such effects the following information shall be taken into consideration:

- (a) studies on toxicity to arthropods;
- (b) information on fate and behaviour in the various parts of the environment;
- (c) available data from biological primary screening.

If mortality or signs of intoxication are observed in the tests the evaluation must include a calculation of toxicity/exposure ratios based on the quotient of the ER<sub>50</sub> value (effective rate) and the estimated exposure.

2.8.5. Member States shall evaluate the possibility of exposure of and effects on earthworms.

2.8.5.1. A micro-organism may give rise to risks because of its potential to infect and multiply in earthworms. Whether or not identified risks could be changed due to the formulation of the plant protection product shall be assessed, taking into account the following information on the micro-organism:

- (a) its mode of action;
- (b) other biological properties;
- (c) studies on earthworm toxicity, pathogenicity and infectivity.

2.8.5.2. A plant protection product may give rise to toxic effects due to the action of toxins or co-formulants. For the assessment of such effects the following information shall be taken into consideration:

- (a) studies on earthworm toxicity;
- (b) information on fate and behaviour in the various parts of the environment.

If mortality or signs of intoxication are observed in the tests the evaluation must include a calculation of toxicity/exposure ratios based on the quotient of the LC<sub>50</sub> value and the estimated exposure expressed in mg/kg dry weight soil.

2.8.6. Member States shall evaluate the possibility of exposure of and effects on soil micro-organisms.

2.8.6.1. A micro-organism may give rise to risks because of its potential to interfere with nitrogen and carbon mineralisation in the soil. Whether or not identified risks could be changed due to the formulation of the plant protection product shall be assessed, taking into account the following information on the micro-organism:

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- (a) its mode of action;
- (b) other biological properties.

Experimental data are not normally required, i.e. where it can be justified that a proper risk assessment can be performed with the available information.

2.8.6.2. Member States shall evaluate the impact of exotic/non-indigenous micro-organisms on non-target micro-organisms and on their predators following use of the plant protection product in accordance with the proposed conditions of use. Experimental data are not normally required, i.e. where it can be justified that a proper risk assessment can be performed with the available information.

2.8.6.3. A plant protection product may give rise to toxic effects due to the action of toxins or co-formulants. For the assessment of such effects the following information shall be taken into consideration:

- (a) information on fate and behaviour in the various parts of the environment;
- (b) all available information from biological primary screening.

2.9. *Conclusions and proposals*

Member States shall draw conclusions on the need for further information and/or testing and the need for measures to limit the risks arising. Member States shall justify proposals for the classification and labelling of plant protection products.

C. DECISION-MAKING

1. **General principles**

- 1.1. Where appropriate, Member States shall impose conditions or restrictions on the authorisations they grant. The nature and severity of these conditions or restrictions must be selected on the basis of, and be appropriate to, the nature and extent of the expected advantages and the risks likely to arise.
- 1.2. Member States shall ensure that decisions taken to grant authorisations, take account of the agricultural, plant health or environmental (including climatic) conditions in the areas of envisaged use. Such considerations may result in specific conditions and restrictions on use, and, in authorisation being granted for some but not other areas within the Member State in question.
- 1.3. Member States shall ensure that the authorised amounts, in terms of rates and number of applications, are the minimum necessary to achieve the desired effect even where higher amounts would not result in unacceptable risks to human or animal health or to the environment. The authorised amounts must be differentiated in accordance with, and be appropriate to, the agricultural, plant health or environmental (including climatic) conditions in the various areas for which an authorisation is granted. However, the rates and the number of applications may not give rise to undesirable effects such as the development of resistance.
- 1.4. Member States shall ensure that decisions respect the principles of integrated pest control if the plant protection product is intended for use in conditions where these principles are relied on.

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- 1.5. Since the evaluation is to be based on data concerning a limited number of representative species, Member States shall ensure that use of plant protection products does not have any long-term repercussions for the abundance and diversity of non-target species.
- 1.6. Before issuing an authorisation, Member States shall ensure that the label of the plant protection product:
- (a) fulfils the requirements setting out in Regulation (EU) No 547/2011;
  - (b) also contains the information on protection of users required by EU legislation on worker protection;
  - (c) specifies in particular the conditions or restrictions under which the plant protection product may or may not be used as referred to in points 1.1 to 1.5;
  - (d) and that the authorisation shall mention the particulars indicated in Annexes II and III to Regulation (EU) 547/2011 and Article 10(1.2), (2.4), (2.5) and (2.6) of Directive 1999/45/EC.
- 1.7. Before issuing authorisations, Member States shall:
- (a) ensure that the proposed packaging is in accordance with the provisions of Directive 1999/45/EC;
  - (b) ensure that:
    - the procedures for destruction of the plant protection product,
    - the procedures for neutralisation of any adverse effects of the plant protection product if it is accidentally dispersed, and
    - the procedures for the decontamination and destruction of the packaging,
 are in accordance with the relevant regulatory provisions.
- 1.8. No authorisation shall be granted unless all the requirements referred to in point 2 are satisfied. However, when one or more of the specific decision-making requirements referred to in point 2.4 are not fully satisfied, authorisations shall be granted only where the advantages of the use of the plant protection product under the proposed conditions of use outweigh the possible adverse effects of its use. Any restrictions on use of the plant protection product relating to non-compliance with some of the requirements referred to in point 2.4 must be mentioned on the label. These advantages can be in terms of:
- (a) advantages for and compatibility with integrated control measures or organic farming;
  - (b) facilitating strategies to minimise the risk of development of resistance;
  - (c) reduced risk for operators and consumers;
  - (d) reduced contamination of the environment and reduced impact on non-target species.
- 1.9. Where an authorisation has been granted in accordance with the requirements provided for in this Annex, Member States may, by virtue of Article 44:
- (a) define, where possible, preferably in close cooperation with the applicant, measures to improve the performance of the plant protection product; and/or
  - (b) define, where possible, in close cooperation with the applicant, measures to reduce further the exposure that could occur during and after use of the plant protection product.

Member States shall inform applicants of any measures identified under (a) or (b) and shall invite applicants to provide any supplementary data and information necessary to demonstrate performance or potential risks arising under the changed conditions.

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- 1.10. Member States shall ensure, as far as is practically possible, that for all micro-organisms that are considered for an authorisation, the applicant has taken into account all available relevant knowledge and information in literature at the time of submission.
- 1.11. Where the micro-organism has been genetically modified, as defined in Directive 2001/18/EC, no authorisation shall be granted unless the evaluation conducted in accordance with Directive 2001/18/EC has been submitted, as required pursuant to Article 53(4) of Regulation (EC) No 1107/2009. The relevant decision taken by the competent authorities in accordance with Directive 2001/18/EC must be provided.
- 1.12. In accordance with Article 53(4) of Regulation (EC) No 1107/2009, no authorisation shall be granted for a plant protection product containing a genetically modified organism unless authorisation is granted in accordance with part C of Directive 2001/18/EC under which that organism can be released into the environment.
- 1.13. No authorisation shall be granted if relevant metabolites/toxins (i.e. those expected to be of concern for human health and/or the environment) known to be formed by the micro-organism, and/or by microbial contaminants are present in the plant protection product, unless it can be shown that the amount present is at an acceptable level before and after its proposed use.
- 1.14. Member States shall ensure that adequate quality control measures are applied to ensure the identity of the micro-organism and contents of the plant protection product. Such measures must include a Hazard Analysis Critical Control Point (HACCP) system or equivalent system.

**2. Specific principles**

The specific principles shall apply without prejudice to the general principles referred to in Section 1.

**2.1. Identity**

For each authorisation granted the Member States shall ensure that the micro-organism concerned is deposited at an internationally recognised culture collection and has an accession number. Each micro-organism must be identified and named at the species level and characterised at the strain level. There must also be information as to whether or not the micro-organism is a wild type or a spontaneous or induced mutant, or a genetically modified organism.

**2.2. Biological and technical properties**

- 2.2.1. There must be sufficient information to permit assessment of the minimum and maximum content of the micro-organism in the material used for the manufacturing of plant protection products, as well as in the plant protection product. The content of other components and formulants in the plant protection product and contaminating micro-organisms derived from the production process must to the extent possible be defined. Member States shall ensure that the level of contaminating organisms is controlled to an acceptable level. In addition: the physical nature and state of the plant protection product must be specified, preferably in accordance with the 'Catalogue of pesticide formulation types and international coding system (CropLife International Technical Monograph No 2, 5th Edition, 2002)'.
- 2.2.2. No authorisation shall be granted if, at any stage in the development of a microbial plant protection product, it becomes apparent, on the basis of a build-up of resistance, or transfer of resistance, or other mechanism, that there may be interference with the effectiveness of an anti-microbial agent used in human or animal medicine.

**2.3. Further information**

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No authorisation shall be granted unless full information is provided on the continuous quality control of the production method, production process and plant protection product. In particular, the occurrence of spontaneous changes in major characteristics of the micro-organism and the absence/presence of contaminating organisms shall be considered. The quality assurance criteria for production and the techniques used to ensure a uniform plant protection product must to the extent possible be described and specified.

**2.4. Efficacy****2.4.1. Performance**

2.4.1.1. No authorisation shall be granted where the proposed uses include recommendations for the control of or protection against organisms which are not considered to be harmful on the basis of experience acquired or scientific evidence under normal agricultural, plant health and environmental (including climatic) conditions in the areas of proposed use or where the other intended effects are not considered to be beneficial under those conditions.

2.4.1.2. The level, consistency and duration of control or protection or other intended effects must be similar to those resulting from the use of suitable reference products. If no suitable reference product exists, the plant protection product must be shown to give a defined benefit in terms of the level, consistency and duration of control or protection or other intended effects under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

2.4.1.3. Where relevant, yield response when the plant protection product is used and reduction of loss in storage must be quantitatively and/or qualitatively similar to those resulting from the use of suitable reference products. If no suitable reference product exists, the plant protection product must be shown to give a consistent and defined quantitative and/or qualitative benefit in terms of yield response and reduction of loss in storage under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use.

2.4.1.4. Conclusions as to the performance of the preparation must be valid for all areas of the Member State in which it is to be authorised, and for all conditions under which its use is proposed, except where the proposed label specifies that the preparation is intended for use in certain specified circumstances (e.g. light infestations, particular soil types or particular growing conditions).

2.4.1.5. Where proposed label claims include requirements for use of the preparation with other specified plant protection products or adjuvants as a tank mix, the mixture must achieve the desired effect and comply with the principles referred to in points 2.4.1.1 to 2.4.1.4.

Where proposed label claims include recommendations for use of the preparation with specified plant protection products or adjuvants as a tank mix, Member States shall not accept the recommendations unless they are justified.

2.4.1.6. If there is evidence of a development of resistance of pathogens towards the plant protection product, the Member State shall decide if the submitted resistance management strategy addresses this adequately and sufficiently.

2.4.1.7. Only plant protection products containing non-viable micro-organisms may be authorised for use to control vertebrate species. The intended effect on vertebrates to be controlled shall be obtained without unnecessary suffering and unnecessary pain for these animals.

**▼B****2.4.2. Absence of unacceptable effects on plants and plant products**

2.4.2.1. There must be no relevant phytotoxic effects on treated plants or plant products except where the proposed label indicates appropriate limitations of use.

2.4.2.2. There must be no reduction of yield at harvest due to phytotoxic effects below that which could be obtained without the use of the plant protection product, unless this reduction is compensated for by other advantages such as an enhancement of the quality of the treated plants or plant products.

2.4.2.3. There must be no unacceptable adverse effects on the quality of treated plants or plant products, except in the case of adverse effects on processing where proposed label claims specify that the preparation should not be applied to crops to be used for processing purposes.

2.4.2.4. There must be no unacceptable adverse effects on treated plants or plant products used for propagation or reproduction, such as effects on viability, germination, sprouting, rooting and establishment, except where proposed label claims specify that the preparation should not be applied to plants or plant products to be used for propagation or reproduction.

2.4.2.5. There must be no unacceptable impact on succeeding crops, except where proposed label claims specify that particular crops, which would be affected, should not be grown following the treated crop.

2.4.2.6. There must be no unacceptable impact on adjacent crops, except where proposed label claims specify that the preparation should not be applied when particular sensitive adjacent crops are present.

2.4.2.7. Where proposed label claims include requirements for use of the preparation with other plant protection products or adjuvants, as a tank mix, the mixture must comply with the principles referred to in points 2.4.2.1 to 2.4.2.6.

2.4.2.8. The proposed instructions for cleaning the application equipment must be both practical and effective so that they can be applied with ease so as to ensure the removal of residual traces of the plant protection product which could subsequently cause damage.

**2.5. *Identification/detection and quantification methods***

The methods proposed must reflect the latest techniques. Methods for post-authorisation monitoring shall involve the use of commonly available reagents and equipment.

2.5.1. No authorisation shall be granted unless there is an adequate method of sufficient quality to identify and quantify the micro-organism and non-viable components (e.g. toxins, impurities and co-formulants) in the plant protection product. In the case of a plant protection product containing more than one micro-organism, the recommended methods should be capable of identifying and determining the content of each one.

2.5.2. No authorisation shall be granted unless there are adequate methods for post-registration control and monitoring of viable and/or non-viable residues. Methods must be available for analysis of:

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- (a) plants, plant products, foodstuffs of plant and animal origin and feedingstuffs if toxicologically relevant residues occur. Residues are considered relevant if a maximum residue level (MRL) or a waiting or re-entry safety period or other such precaution is required;
- (b) soil, water, air and/or body tissues if toxicologically, ecotoxicologically or environmentally relevant residues occur.

2.6. *Impact on human and animal health*

## 2.6.1. Effects on human and animal health arising from the plant protection product

2.6.1.1. No authorisation shall be granted if on the basis of the information provided in the dossier it appears that the micro-organism is pathogenic to humans or non-target animals under the proposed conditions of use.

2.6.1.2. No authorisation shall be granted if the micro-organism and/or the plant protection product containing the micro-organism might, under the recommended conditions of use, including a realistic worst case scenario, colonise or cause adverse effects in humans or animals.

When making a decision on the authorisation of the microbial plant protection product, Member States shall consider possible effects on all human populations, namely professional users, non-professional users and humans exposed directly or indirectly through the environment and at work, and animals.

2.6.1.3. All micro-organisms shall be regarded as potential sensitisers, unless it is established by means of relevant information that there is no risk of sensitisation, taking into account immuno-compromised and other sensitive individuals. Authorisations granted shall therefore specify that protective clothing and suitable gloves be worn and that the plant protection product containing the micro-organism shall not be inhaled. Moreover, the proposed conditions of use may require use of additional items of protective clothing and equipment.

Where the proposed conditions of use require use of items of protective clothing, no authorisation shall be granted unless those items are effective and in accordance with relevant EU provisions, and are readily obtainable by the user and unless it is feasible to use them under the conditions of use of the plant protection product, taking into account climatic conditions in particular.

2.6.1.4. No authorisation shall be granted if it is known that transfer of genetic material from the micro-organism to other organisms may lead to adverse effects on human and animal health, including resistance to known therapeutic substances.

2.6.1.5. Plant protection products which, because of particular properties, or which, if mishandled or misused, could lead to a high degree of risk must be subject to particular restrictions such as restrictions on the size of packaging, formulation type, distribution, use or manner of use. Moreover, plant protection products which are classified as very toxic shall not be authorised for use by non-professional users.

2.6.1.6. Waiting and re-entry safety periods or other precautions must be established in such a way that no colonisation of or adverse effects on bystanders or workers exposed after application of the plant protection product are expected.

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- 2.6.1.7. Waiting and re-entry safety periods or other precautions must be established in such a way that no colonisation of or adverse effects on animals are expected.
- 2.6.1.8. Waiting and re-entry periods or other precautions to ensure that no colonisation or adverse effects are expected must be realistic; if necessary, special precautionary measures must be prescribed.
- 2.6.1.9. The conditions of authorisation shall be in compliance with Directive 98/24/EC and Directive 2000/54/EC of the European Parliament and of the Council <sup>(1)</sup>. The experimental data and information relevant to the recognition of the symptoms of infection or pathogenicity and on the effectiveness of first aid and therapeutic measures provided shall be considered. The conditions of authorisation shall also be in compliance with Directive 2004/37/EC. The conditions of authorisation shall also be in compliance with Council Directive 89/656/EEC <sup>(2)</sup>.
- 2.6.2. Effects on human and animal health arising from residues
- 2.6.2.1. No authorisation shall be granted unless there is sufficient information for plant protection products containing the micro-organism, to decide that there is no harmful effect on human or animal health arising from exposure to the micro-organism, its residual traces and metabolites/toxins remaining in or on plants or plant products.
- 2.6.2.2. No authorisation shall be granted unless viable residues and/or non-viable residues occurring reflect the minimum quantities of the plant protection product necessary to achieve adequate control corresponding to good agricultural practice, applied in such a manner (including pre-harvest intervals or withholding periods or storage periods) that the viable residues and/or toxins at harvest, slaughter or after storage are reduced to a minimum.
- 2.7. *Fate and behaviour in the environment*
- 2.7.1. No authorisation shall be granted if the available information indicates that there may be unacceptable adverse environmental effects due to the fate and behaviour of the plant protection product in the environment.
- 2.7.2. No authorisation shall be granted if contamination of ground water, surface water or drinking water expected as a result of the use of a plant protection product under the proposed conditions of use, may cause interference with the analytical systems for the control of the quality of drinking water provided for in Directive 98/83/EC.
- 2.7.3. No authorisation shall be granted if the contamination of groundwater expected as a result of the use of a plant protection product under the proposed conditions of use contravenes or exceeds whichever of the following is the lower:
- (a) the parameters or maximum permissible concentrations laid down by Directive 98/83/EC; or
  - (b) the parameters or maximum permissible concentrations laid down for components in the plant protection product such as relevant metabolites/toxins in accordance with Directive 2000/60/EC; or
  - (c) the parameters for the micro-organism or the maximum concentration laid down for components in the plant protection product such as relevant metabolites/toxins when approving the micro-organism in accordance with Regulation (EC) No 1107/2009, on the basis of appropriate data, in particular, toxicological data, or,

<sup>(1)</sup> OJ L 262, 17.10.2000, p. 21.

<sup>(2)</sup> OJ L 393, 30.12.1989, p. 18.

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where that concentration has not been laid down, the concentration corresponding to 1/10 of the acceptable daily intake (ADI) laid down when the micro-organism was approved in accordance with Regulation (EC) No 1107/2009,

unless it is scientifically demonstrated that under relevant field conditions the lower of the parameters or concentrations is not contravened or exceeded.

2.7.4. No authorisation shall be granted if the contamination of surface water expected as a result of the use of a plant protection product under the proposed conditions of use:

- (a) exceeds, where the surface water in or from the area of envisaged use is intended for the extraction of drinking water, concentrations above which compliance with drinking water quality established in accordance with Directive 2000/60/EC is compromised; or
- (b) exceeds the parameters or values for components in the plant protection product, such as relevant metabolites/toxins, established in accordance with Directive 2000/60/EC; or
- (c) has an impact deemed unacceptable on non-target species, including animals, in accordance with the relevant requirements provided for in point 2.8.

The proposed instruction for use of the plant protection product, including procedures for cleaning application equipment, must be such that the likelihood of accidental contamination of surface water is reduced to a minimum.

2.7.5. No authorisation shall be granted if it is known that transfer of genetic material from the micro-organism to other organisms, may lead to unacceptable effects on the environment.

2.7.6. No authorisation shall be granted unless there is sufficient information on the possible persistence/competitiveness of the micro-organism and relevant secondary metabolites/toxins in or on the crop under the environmental conditions prevailing at and following the intended use.

2.7.7. No authorisation shall be granted if it can be expected that the micro-organism and/or its possible relevant metabolites/toxins shall persist in the environment in concentrations considerably higher than the natural background levels, taking into account repeated applications over the years, unless a robust risk assessment indicates that the risks from accumulated plateau concentrations are acceptable.

2.8. *Effects on non-target organisms*

Member States shall ensure that the available information is sufficient to permit a decision to be taken as to whether or not there may be unacceptable effects on non-target species (flora and fauna), due to exposure to the plant protection product containing the micro-organism following its intended use.

Member States shall pay special attention to possible effects on beneficial organisms used for biological control and organisms playing an important role in integrated control.

2.8.1. Where there is a possibility of birds and other non-target terrestrial vertebrates being exposed, no authorisation shall be granted if:

- (a) the micro-organism is pathogenic to birds and other non-target terrestrial vertebrates;
- (b) in case of toxic effects due to components in the plant protection product, such as relevant metabolites/toxins, the toxicity/exposure ratio is less than 10 on the basis of the acute LD<sub>50</sub> value or the long-term toxicity/exposure ratio is less than 5, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable effects occur — directly or indirectly — after use of the plant protection product in accordance with the proposed conditions of use.

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- 2.8.2. Where there is a possibility of aquatic organisms being exposed, no authorisation shall be granted if:
- (a) the micro-organism is pathogenic to aquatic organisms;
  - (b) in case of toxic effects due to components in the plant protection product such as relevant metabolites/toxins, the toxicity/exposure ratio is less than 100 in case of acute toxicity ( $EC_{50}$ ) to daphnia and fish and 10 for long-term/chronic toxicity to algae ( $EC_{50}$ ), daphnia (NOEC) and fish (NOEC), unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact on the viability of exposed species occurs — directly or indirectly — after use of the plant protection product in accordance with the proposed conditions of use.
- 2.8.3. Where there is a possibility of bees being exposed, no authorisation shall be granted:
- (a) if the micro-organism is pathogenic to bees;
  - (b) in case of toxic effects due to components in the plant protection product such as relevant metabolites/toxins, the hazard quotients for oral or contact exposure of honeybees are greater than 50, unless it is clearly established through an appropriate risk assessment that under field conditions there are no unacceptable effects on honeybee larvae, honeybee behaviour, or colony survival and development after use of the plant protection product in accordance with the proposed conditions of use.
- 2.8.4. Where there is a possibility of arthropods other than bees being exposed, no authorisation shall be granted if:
- (a) the micro-organism is pathogenic to arthropods other than bees;
  - (b) in case of toxic effects due to components in the plant protection product such as relevant metabolites/toxins, unless it is clearly established through an appropriate risk assessment that under field conditions there is no unacceptable impact on those organisms after use of the plant protection product in accordance with the proposed conditions of use. Any claims for selectivity and proposals for use in integrated pest management systems shall be substantiated by appropriate data.
- 2.8.5. Where there is a possibility of earthworms being exposed, no authorisation shall be granted if the micro-organism is pathogenic to earthworms or in the case of toxic effects due to components in the plant protection product such as relevant metabolites/toxins, the acute toxicity/exposure ratio is less than 10, or the long-term toxicity/exposure ratio is less than 5, unless it is clearly established through an appropriate risk assessment that under field conditions earthworm populations are not at risk after use of the plant protection product in accordance with the proposed conditions of use.
- 2.8.6. Where there is a possibility of non-target soil micro-organisms being exposed, no authorisation shall be granted if the nitrogen or carbon mineralisation processes in laboratory studies are affected by more than 25 % after 100 days, unless it is clearly established through an appropriate risk assessment that under field conditions there is no unacceptable impact on the microbial community after use of the plant protection product in accordance with the proposed conditions of use, taking account of the ability of micro-organisms to multiply.