S.I. No. 83 of 2003

EUROPEAN COMMUNITIES (AUTHORIZATION, PLACING ON THE MARKET, USE AND CONTROL OF PLANT PROTECTION PRODUCTS) REGULATIONS 2003

TABLE OF CONTENTS

Contents of Statutory Instrument

38 Revocations

39 Savers

S.I. No. 83 of 2003

EUROPEAN COMMUNITIES (AUTHORIZATION, PLACING ON THE MARKET, USE AND CONTROL OF PLANT PROTECTION PRODUCTS) REGULATIONS 2003

I, Joe Walsh, Minister for Agriculture and Food, in exercise of the powers conferred on me by section 3 of the European Communities Act, 1972 (No. 27 of 1972), for the purpose of giving effect to Council Directive 91/414/EEC of 15 July 1991 [1], the Corrigendum to Council Directive 91/414/EEC [2], Council Directive 97/57/EC of 22 September 1997 [3], Commission Directive 93/71/EEC of 27 July 1993[4], the Corrigendum to Commission Directive 93/71/EEC [5], Commission Directive 94/37/EC of 22 July 1994 [6], Commission Directive 94/79/EC of 21 December 1994 [7], the Corrigendum to Commission Directive 94/79/EEC [8], Commission Directive 95/35/EC of 14 July 1995 [9], Commission Directive 95/36/EC of 14 July 1995 [10], Commission Directive 96/12/EC of 8 March 1996 [11], Commission Directive 96/46/EC of 16 July 1996 [12], Commission Directive

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[1] O.J. No. L230 19/8/1991 p1

[2] O.J. No. L170 25/6/1992 p40

[3] O.J. No. L265 27/9/1997 p87

[4] O.J. No. L221 31/8/1993 p27

[5] O.J. No. L4 6/1/1996 p16

[6] O.J. No. L194 29/7/1994 p65

[7] O.J. No. L354 31/12/1994 p16

[8] O.J. No. L280 23/11/1995 p58

[9] O.J. No. L172 22/7/1995 p6

[10] O.J. No. L172 22/7/1995 p8

[11] O.J. No. L65 15/3/1996 p20

96/68/EC of 21 October 1996 [13], Commission Directive 2000/80/EC of 4 December 2000 [14], Commission Directive 2001/21/EC of 5 March 2001 [15], Commission Directive 2001/28/EC of 20 April 2001 [16], Commission Directive 2001/47/EC of 25 June 2001 [17], Commission Directive 2001/49/EC of 28 June 2001 [18], Commission Directive 2001/87/EC of 12 October 2001[19], Commission Directive 2001/99/EC of 20 November 2001[20], Commission Directive 2001/36/EC of 16 May 2001 [21], Commission Directive 2001/103/EC of 28 November 2001 [22], Commission Directive 2002/18/EC of 22 February 2002 [23], Commission Directive 2002/37/EC of 3 May 2002 [24], Commission Directive 2002/48/EC of 30 May 2002 [25] Commission Directive 2002/64/EC of 15 July 2002 [26], and Commission Directive 2002/81/EC of 10 October 2002[27] hereby make the following regulations:

Citation

1 These Regulations may be cited as the European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) Regulations 2003.

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[12] O.J. No. L214 3/8/1996 p18
[13] O.J. No. L227 30/10/1996 p25
[14] O.J. No. L309 9/12/2000 p14
[15] O.J. No. L69 10/3/2001 p17
[16] O.J. No. L113 24/4/2001 p5
[17] O.J. No. L175 28/6/2001 p21
[18] O.J. No. L176 29/6/2001 p61
[19] O.J. No. L276 19/10/2001 p17
[20] O.J. No. L304 21/11/2001 p14
[21] O.J. No. L164 20/6/2001 p1
[22] O.J. No. L313 30/11/2001 p37
[23] O.J. No. L55 of 26/2/2002 p29
[24] O.J. No. L117 of 4/5/2002 p10
[25] O.J. No. L148 of 6/6/2002 p19
[26] O.J. No. L189 of 18/7/2002 p20
[27] O.J. No. L276 of 12/10/2002 p28
[28] O.J No. L8 of 14/01/2003 p7

Interpretation

2 (1) In these Regulations –

"actual conditions of use" in relation to good agriculture practice includes any stage in the production, storage, transport and distribution of plants and plant products;

"aircraft" includes hovercraft;

"authorized officer" means a person appointed in writing under Regulation 29;

"Commission" means the Commission of the European Communities;

"designated analyst" means any appropriately qualified person who is authorized in writing under Regulation 30;

"Directive of 1967" means Council Directive 67/548/EEC of 27 June, 1967 [29], as amended and adapted;

"Directive of 1991" means Council Directive No. 91/414/EEC of 15 July 1991;

"Directive of 1992" means Council Directive 92/32/EC of 30 April 1992 [30];.

"Directive of 1999" means Directive 1999/45/EC of the European Parliament and of the Council of 31 May 1999 [31] and the corrigendum to Directive 1999/45/EC [32];

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[29] O.J. No. L196/1 16/8/1967

[30] O.J. No. L154/1 5/6/1992

[31] O.J. No. L200/1 30/7/1999

[32] O.J. No. L6/70 10/1/2002

"essential use" means a use of a plant protection product for which there is no practical alternative available or for which there are an insufficient number of suitable alternatives available;

"good agricultural practice" in the use of a plant protection product, means safe use of the plant protection product under actual conditions necessary for its effective action, in accordance with an authorization granted pursuant to these Regulations, encompassing a range of levels of application up to the highest level of use for which an authorization has been granted, applied in a manner which leaves a residue which is the smallest practicable;
"good plant protection practice" in the use of plant protection products, means their responsible use in accordance with the guidelines issued from time to time by the Minister,

“insufficient number of suitable alternatives”, in relation to essential use means insufficient to avoid the imposition of selective pressure for the development of resistant populations of harmful organisms;

‘ISO.’ means the International Organisation for Standardisation;

‘IUPAC Rules’ means the chemical nomenclature rules adopted by the International Union of Pure and Applied Chemistry;

“maximum residue level” is the maximum content of residual traces of a plant protection product contained in a product to which a plant protection product has been applied;

"Member State" means a Member State of European Communities;

"Minister” means the Minister for Agriculture and Food;

"notified" means the packaging, including any label or container used with the package, and basic information as to the nature and composition of any such plant protection product on the market on or before the 2nd December 1985 and the manufacturer of each plant protection product which has been submitted and approved by the Minister under the Regulations of 2001, and cognate words shall be construed accordingly,

“notified” in the case of an adjuvant for use with a plant protection product or a plant protection product containing a macro-organism means

a) the packaging, including any label or container used with the package,

b) basic documentation,
c) information as to the nature and composition of any such adjuvant or plant protection product,

and as to the producer or manufacturer of each such adjuvant or plant protection product, has been submitted to and been approved by the Minister and cognate words shall be construed accordingly,

"officially recognized testing facilities and organizations" for the purposes of these Regulations, means testing facilities and organizations which carry out officially recognised tests and analyses,

"officially recognized tests and analyses" for the purposes of these Regulations, means experiments, studies, tests and analyses carried out in accordance with methodologies and to a standard accepted from time to time by the Minister and issued as guideline documentation,

"parallel import approval" means an approval granted by the Minister for the importation, distribution, sale and use of a plant protection product deemed identical to a product on the register of plant protection products that may be placed on the market and used in accordance with these regulations,

"permission to market" means a permission granted by the Minister to place on the market and use a plant protection product;

"register of plant protection products" means a list established under Regulation 21;

"Regulations of 2001" means the European Communities (Classification, Packaging and Labelling of Plant Protection Products and Biocide Products) Regulations, 2001 (S.I. No. 624 of 2001);

“safe use, in relation to good agricultural practice”, means taking into account public and occupational health and environmental considerations;

“trials authorization” means an authorization granted in accordance with Regulation 24

“trials permit” means a permit granted in accordance with Regulation 25

(2) A word or expression that is used in the Directive of 1991 or in or Commission Directive or Regulation of the European Communities mentioned in these Regulations has, unless the contrary intention appears, the meaning in these Regulations that it has in the Directive or Regulation concerned

(3) In these Regulations, unless otherwise indicated -

(a) a reference to a Regulation is a reference to a Regulation of these Regulations,

(b) a reference to a paragraph or subparagraph is a reference to a paragraph or subparagraph of the provision in which the reference occurs,

(c) a reference to a Schedule is a reference to the Schedule to these Regulations.

(4) A reference to a Directive is to the Directive as amended or extended.

Application

3. (1) Subject to paragraph (2), these Regulations apply to the production, storage or movement of a plant protection product

(2) These Regulations do not apply to a plant protection product intended for use in another Member State and Regulations 32 and 33 are complied with.

Placing on the market

4. (1) A person shall not place a plant protection product on the market, cause or permit another person to place a plant protection product on the market, use the product or cause or permit another person to use the product unless these Regulations are complied with.

(2) A person shall not place a plant protection product on the market if -

(a) the net quantity of a plant protection product in a container is less than the quantity stated on the container, or

(b) a fastening or container used to package the plant protection product has been tampered with.

Exemptions from certain provisions

5 (1) A plant protection product referred to in Regulation 3 (1) (a) of the Regulations of 2001, classified in accordance with those Regulations is -

(a) exempt from
  (i) Regulation 11 (2) (a) and (b), and
  (ii) Regulation 25 of the Regulations of 2001,
and

(b) considered to comply with –
  (i) Regulation 11 (1), and
  (ii) Regulations 12 and 13 of the Regulations of 2001,

where it has been authorized under these Regulations.

(2) A plant protection product referred to in Regulation 3 (1) (a) of the Regulations of 2001 that is on the market before the making of these Regulations may continue to be placed on the market under the Regulations of 2001, until:-

(a) approval of the record of the studies conducted and the information, documentation and materials submitted for approval under Regulation 11 (2) (a) or (b) of the Regulations of 2001 has been refused and clearance under those Regulations has been refused, or

(b) it is authorized or is refused an authorization under these Regulations.

(3) Notwithstanding Regulations 8, 13 and 18, in the case of a plant protection product which is not on the market before these Regulations come into effect, permission may be granted by the Minister on approval of an accurate record of studies, information, supporting documentation and materials, as set out from time to time by the Minister, to market and use such a plant protection product, where application is made and -

(a) the plant protection product is similar in terms of its active substance or active substances to one or more plant protection products placed on the market in accordance with these Regulations, and the proposed uses of the plant protection product are encompassed by those of the product or products with which comparison is made,

(b) the plant protection product contains at least one active substance not present in a plant protection product authorized in accordance with these Regulation,

(c) at least one active substance in the plant protection product is included in the review programme for existing active substances pursuant to Article 8.2 of the Directive of 1991 and has not yet been included in Annex I,

(d) none of the active substances in the plant protection product have been refused inclusion in Annex I,

(e) the plant protection product warrants the same or a less severe hazard classification than the plant protection product or products referred to in subparagraph (a),

(f) the plant protection product is considered to involve no greater risk for man, animals or for the environment than the plant protection product or products referred to in subparagraph (a), and

(g) where comparison is made with two or more plant protection products used as a tank mix, the approved label for one of the products must include a recommendation for such tank-mixing,

unless the periods specified in Regulation 10 have not yet expired for information referred to in Regulation 8 (3) (a) and (b).

(4) Notwithstanding Regulations 13 and 18, in the case of a plant protection product for which an application for authorization has been made under Regulation 8, authorization for a period not exceeding 12 months may be granted if -

(a) (i) the active substance in the plant protection product is included in Annex I to the Directive of 1991,

(ii) a detailed assessment of the data referred to in Regulation 8 (4) (a) and (b) prepared by the competent authority of the other Member State responsible for its evaluation on behalf of the Commission is available to the Minister, or

(iii) a detailed assessment comparable to that referred to in subparagraph (ii) prepared by another Member State is available to the Minister,

(b) an active substance in a plant protection product has not been refused inclusion in Annex I to the Directive of 1991,

(c) the plant protection product has been authorized for use in another Member State and a copy of the certificate of authorization and of the approved label in that Member State for the plant protection product is provided to the Minister,

(d) a proposed use of a plant protection product is –

(i) a use considered for the purposes of including an active substance in Annex I to the Directive of 1991, or

(ii) a use considered for assessment as referred to in subparagraph (a),

(e) in the opinion of the Minister there is a reasonable expectation that an authorization will be granted under Regulation 13 or 18 before expiry of the authorization, and

(f) at least one of the uses for which authorization is sought is considered, in the opinion of the Minister, to be an essential use.

Use of plant protection products

6 A person shall only use a plant protection product -

(a) in compliance with conditions established under Regulations 13, 15, 18 and 19 and stated on the label, as appropriate,

(b) in compliance with conditions established under Regulation 16, as appropriate,

(c) in the case of plant protection products on the market before these Regulations come into effect and pending their authorization in accordance with these Regulations, in compliance with the conditions specified on the labelling, approved following the granting of clearance, permission to market or accepted for their notification, as appropriate,

(d) in accordance with the principles of good plant protection practice, and

(e) where possible, in accordance with the principles of integrated control.

Marketing of active substances

7. (1) A person shall only place an active substance on the market where -

(a)it is classified, packaged and labelled under the Directive of 1967, and

(b) where the active substance was not on the market before 25 July 1993 a dossier has been forwarded to the Member States and the Commission, in accordance with Article 6 of the Directive of 1991, with the declaration that the active substance is intended for a use specified in Article 2 (1) of that Directive.

(2) This Regulation shall not apply to an active substance contained in a plant protection product intended for use for trial purposes in accordance with Regulations 25 and 26.

Application for authorization

8 (1) An application for authorization shall be made by or on behalf of the person responsible for first placing it on the market.

(2) An applicant for an authorization shall be established in a Member State.

(3) An application shall be in such form and contain such information as the Minister may require.

(4) An application for authorization of a plant protection product shall include -

a) a dossier satisfying, in the light of current scientific and technical knowledge, the requirements set out in Annex III of the Directive of 1991,

b) for each active substance in the plant protection product, a dossier satisfying, in the light of current scientific and technical knowledge, the requirements set out in Annex II of the Directive of 1991,

c) samples of the packaging and models, drafts or samples of labelling and leaflets referred to in Regulations 22 and 23

d) samples of the plant protection products and each active substance therein in it and analytical standards for each such active substance,

i. for impurities and formulants of toxicological or environmental significance, and

ii. for transformation products of the active substance included in the residue definition, and

e) any other matter that the Minister may require.

(5) The tests and analyses conducted for the purposes of compiling dossiers referred to in paragraph (4) (a), shall be

a. carried out under agricultural, plant health and environmental conditions relevant to use of the plant protection product in question and
b. representative of those prevailing where the product is intended to be used,
c. and shall be officially recognized tests and analyses

(6) Notwithstanding paragraph (3) and subject to Regulation 10 -

(a) an applicant is exempt from supplying information required under paragraph 4 (b), except for that identifying the active substance, if the active substance is already listed in Annex I to the Directive of 1991, taking into account the conditions of inclusion in Annex I to the Directive of 1991, and does not differ significantly in degree of purity and nature of impurities, from the composition registered in the Annex II to the Directive of 1991 dossier accompanying the original application, and

(b) in the case of a plant protection product already authorized in another Member State, at the request of an applicant, who must substantiate the claim to comparability with documentary evidence, an applicant shall be exempted from repeating tests and analyses already carried out in connection with the authorization of the product, to the extent that agricultural, plant health and environmental (including climatic) conditions relevant to the use of the product are comparable in the regions concerned.

(7) Subject to Regulation 10, an application for authorization of a plant protection product in accordance with Regulation 13 (2), taking account of the agricultural, plant health and environmental (including climatic) conditions relevant to the use of the product in the regions concerned, shall be supported with a claim as to the comparability of the regions concerned and shall be supported with documentary evidence to support any such claim.

(8) The Minister shall not consider an incomplete application.

Limiting of testing involving vertebrate species

9. (1) Notwithstanding Regulations 8 and 10, an applicant for authorization of a plant protection product shall, before carrying out experiments involving vertebrate animals, enquire of the Minister -

(a) whether the plant protection product for which an application is to be made is the same as a plant protection product for which authorization has been granted, and

(b) as to the name and address of the authorization holder.

(2) If the Minister is satisfied on the basis of documentary evidence provided that the prospective applicant intends to apply for authorization on his or her own behalf and that the other information specified in Regulation 8 (4) is available to him or her for use on his or her behalf, the Minister shall provide the name and address of any holder of a previous relevant authorization and shall at the same time inform that holder of the name and address of the applicant.

(3) The holder of a previous authorization and the applicant shall take all reasonable steps to reach agreement on the sharing of information so as to avoid the duplication of testing on vertebrate animals.

(4) If data is to be submitted with a view to inclusion in Annex I to the Directive of 1991 of an active substance on the market after 24 July 1993, the Minister shall encourage applicants to cooperate in the provision of the requested data, with a view to limiting the duplication of testing on vertebrate animals.

(5) If application is made for the inclusion in Annex I to the Directive of 1991 of an active substance on the market after 24 July 1993, an applicant shall take all reasonable steps to reach agreement on -

(a) sharing of relevant data and information, and

(b) submission collectively of all the data and information concerned.

(6) This Regulation is in addition to and not in substitution for the Cruelty to Animals Act 1876[33]

[33] 1876, c. 77).

Proprietary rights to data

10 (1) Information contained in a dossier referred to in Regulation 8 (4) (b) shall not be used to the benefit of another applicant unless -

(a) the applicant has agreed with the first applicant that use may be made of the information and the first applicant has submitted written confirmation of the agreement, or

(b) 10 years have elapsed from the first inclusion in Annex I to the Directive of 1991 of an active substance first placed on the market in a Member State as a constituent of a plant protection product after 24 July 1993, or

(c) 10 years have elapsed from the date of first marketing within the territory of the State of an active substance as a constituent of a plant protection product which was on the market before 25 July 1993, and

(d) Subject to paragraph (2), 5 years have elapsed from the date of decision in the case of further information that is generated specifically for and is necessary -

(i) for first inclusion of an active substance in Annex I to the Directive of 1991, or

(ii) to vary the conditions for, or to maintain, the inclusion of an active substance in Annex I to the Directive of 1991.

(2) If the period of 5 years provided for in paragraph (1)(d) expires before the periods provided for in paragraphs (1) (b) and (c) the period of 5 years shall be extended so as to expire on the same date as those periods.

(3) Information contained in a dossier referred to in Regulation 8 (4) (a) shall not be used to the benefit of another applicant unless -

(a) the applicant has agreed with the first applicant that use may be made of the information and the first applicant has submitted written confirmation of the agreement,

(b) 10 years have elapsed from the first authorization or marketing of the plant protection product in any Member State, where authorization follows the inclusion in Annex I to the Directive of 1991 of any active substance contained in the product, or

(c) 10 years have elapsed from the date of first marketing within the territory of the State of a plant protection product where such marketing precedes inclusion in Annex I to the Directive of 1991 of any active substance contained in the product.

(4) Paragraphs (1), (2) and (3) apply to data and information submitted under the Regulations of 2001.

Confidentiality

11 (1) An applicant for authorization of a plant protection product, who claims that certain information submitted in accordance with Regulation 8, includes information involving industrial or commercial secrets, may apply for the information to be treated as confidential.

(2) An application shall identify the information concerned and shall include a statement justifying the application that it be treated as confidential.

(3) Subject to paragraphs (5) and without prejudice to Council Directive 90/313/EEC of 7 June 1990[34], the Minister shall ensure that information referred to in paragraph (1) is treated as confidential where he or she shall accepts that such treatment is justified.

(4) Confidentiality shall not apply to -

(b) the name and content of an active substance;

(c) the name of the plant protection product,

[34] O.J. No. L158/56 23/6/1990

(c) the name of any other substance which is regarded as dangerous under the Directive of 1967 or the Directive of 1999,

(d) physico-chemical data concerning the active substance and plant protection product,

(e) any method of rendering the active substance or plant protection product harmless,

(f) a summary of the results of tests to establish the efficacy of the substance or product and harmlessness to humans, animals, plants or the environment,

(g) any recommended method and precautions to reduce handling, storage, transport, fire or other hazards,

(h) any method of analysis accepted under Article 4(1)(c) and (d) and 5(1) of the Directive of 1991,

(i) any method of disposal of a product or its packaging,

(j) any decontamination procedure to be followed in the case of accidental spillage or leakage, or

(k) first aid and medical treatment to be given in the case of injury to persons.

(5) If an applicant discloses previously confidential information, he or she shall inform the Minister of the fact.

Consideration of applications

12 (1) The Minister shall consider a completed application for authorization of a plant protection product and inform the applicant within a reasonable period, of his or her decision to authorize the product or refuse the application.

(2) In the case of applications involving one or more active substances not on the market in a Member State as a constituent of a plant protection product after 24 July 1993 and not subsequently included in Annex I to the Directive of 1991, the Minister shall, without undue delay, assess the information provided to determine if the requirements specified in Regulation 8 (4) have been satisfied.

(3) For each such application referred to in Paragraph (2) believed to satisfy the requirements of Annex II to the Directive of 1991, the Minister shall require the applicant to forward the dossier to the other Member States and to the Commission together with a dossier complying with Annex III to the Directive of 1991 on at least one preparation containing that active substance.

(4) If, under paragraph (3), an applicant is required to forward a dossier believed to satisfy Annex II to the Directive of 1991 a dossier complying with Annex III to the Directive of 1991 on at least one preparation containing the active substance, the Minister shall, under Article 6.3 of the Directive of 1991, request the Commission to establish whether the dossier satisfies Annex II and Annex III to the Directive of 1991, under the procedure provided for in that Article.

Granting of authorizations

13 (1) Subject to Regulation 19 and paragraph (3) the Minister shall only authorize the placing on the market and use of any plant protection product where -

(a) each active substance contained in the product is listed in Annex I to the Directive of 1991 and any condition laid down therein is fulfilled,

(b) following application of Annex VI to the Directive of 1991, Article 4 (1) (b), (c), (d) and (e) of the Directive of 1991 are satisfied,

(c) where relevant, maximum residue levels in the agricultural products referred to in the authorization have been established and notified to the Commission, and

(d) its packaging and labelling satisfy Regulations 22 and 23;

(2) Subject to paragraphs (3) and (4), if a plant protection product, authorized under the Directive of 1991 in another Member State, contains only active substances included in Annex I to the Directive of 1991, at the request of the applicant, the Minister, to the extent that Annex VI to the Directive of 1991 has been adopted under Article 23 of the Directive of 1991, may authorize the placing on the market and use

of the product, if it has been established to the satisfaction of the Minister that the agricultural, plant health and environmental (including climatic) conditions relevant to the use of the product are comparable in the regions concerned.

(3) The Minister may impose conditions and restrictions on use to avoid exposure of consumers to risks of dietary contamination in excess of the acceptable daily intake of a residue of a plant protection product and to take account of differences in dietary patterns.

(4) An authorization granted under this Regulation may, with the agreement of the applicant, be subject to changes in the conditions of use in order to render, in the regions concerned, any non-comparable agricultural, plant health or environmental (including climatic) conditions irrelevant for the purpose of comparability.

(5) The Minister may attach such conditions and restrictions to an authorization, as are, in his or her opinion, necessary and relevant to ensure:

(a) compliance with Article 4 (1) (b) of the Directive of 1991, and

(b) that maximum residue levels are not exceeded.

(6) An authorization granted under this Regulation shall be valid for a period not exceeding 10 years.

Refusal to recognize comparability

14 (1) Where the Minister does not accept that claims as to comparability, with respect to the agricultural, plant health and environmental (including climatic) conditions relevant to use of the product in the regions concerned, made in accordance with Regulation 8 (6) (b), are justified, and has required the repetition of one or more tests and analyses, he or she shall notify the Commission of the grounds on which the repetition of tests or analysis is required.

(2) Where the Minister does not accept that claims as to comparability, with respect to the agricultural, plant health and environmental (including climatic) conditions relevant to use of the product in the regions concerned, made in accordance with Regulation 8 (7) are justified, and has refused to authorize a plant protection product in accordance with Regulation 13 (2), it shall notify the Commission of the grounds on which the application was refused.

(3) Where a decision different from that of the Minister is made pursuant to Article 10 (3) of the Directive of 1991, he or she shall without delay accept the tests and analyses or authorize the placing of the plant protection product on the market, subject in the latter case to any terms which the above decision may set.

Authorization for provisional periods

15. (1) Notwithstanding Regulation 13 (1) (a) and subject to Regulation 19, a person may apply, under Regulation 8 for an authorization for a provisional period for the placing on the market and use of a plant protection product containing an active substance not listed in Annex I to the Directive of 1991 and not available on the market after 24 July 1993.

(2) The Minister may grant an authorization to which paragraph (1) refers for a period not exceeding three years, if -

(a) following application of Article 6 (2) and (3) of the Directive of 1991, it is found that the dossier on the active substance satisfies Annexes II and III of the Directive of 1991 in relation to the projected uses,

(b) the active substance satisfies Article 5 (1) of the Directive of 1991 and that the plant protection product may, in the opinion of the Minister, be expected to satisfy Regulation 13 (1) (b) and (c); and

(c) its packaging and labelling satisfy Regulations 22 and 23.

(3) Notwithstanding paragraph (2), where on expiry of the authorization, a decision has not been taken concerning the inclusion of an active substance in Annex I to the Directive of 1991, the Minister may grant a further period of provisional authorization.

Extension of the field of application of a plant protection product

16. (1) An official or scientific body involved in agricultural activities, a professional agricultural organisation or a professional user may request that the field of application of a plant protection product included on the register of plant protection products, be extended to purposes other than those covered by the authorization, clearance, permission to market or notification concerned

(2) Subject to paragraph (4), the Minister may grant an extension of the field of application of a product included in the register of plant protection products, where -

(a) an application for an extension of the field of its application is made in a form and containing documentation and information, as the Minister may require from time to time,

(b) the Minister has established that the conditions referred to in Article 4 (1) (b) (iii), (iv) and (v) of the Directive of 1991, are satisfied, and

(c) the extension of the field of application relates to one or more minor uses.

(3) The Minister shall post on the official Pesticide Control Service internet site or by other means, information on the extended use of the plant protection product.

(4) An extension expires on the same date as the authorization, permission to market, clearance or notification for the plant protection product to which it relates.

Information on potentially harmful effects

17. (1) A person to whom an authorization, an extension or a permission to market under has been granted, shall immediately notify the Minister of all new information on potentially dangerous effects of a plant protection product or of residues of an active substance contained in a plant protection product on human or animal health, ground water or the environment.

(2) A person who makes notification under paragraph (1) shall immediately notify the information provided to the other Member States and to the Commission.

Authorization of certain plant protection products on the market before 25 July 1993

18. (1) Subject to paragraph (3) and Regulation 19 (7), before 25 July 2003, an application may be made to the Minister for authorization of a plant protection product under Regulation 8 in respect of a product containing an active substance not listed in Annex I to the Directive of 1991 that was on the market before 25 July 1993.

(2) Pending the review of the active substances under Article 8 (2) of the Directive of 1991, an application made under paragraph (1) shall be examined by the Minister who will decide thereon within a reasonable period.

(3) In deciding on an application under paragraph (1), the Minister shall only authorize the placing on the market and use of a plant protection product if -

(a) following application of Annex VI to the Directive of 1991, the requirements of Article 4 (1) (b), (c), (d) and (e) of the Directive of 1991 are satisfied,

(b) where relevant, a maximum residue level in the agricultural products referred to in the authorization has been notified to the Commission, and

(c) its packaging and labelling satisfy Regulations 22 and 23;

Renewal, alteration and cancellation of authorizations

19 (1) Where an application is made for the renewal of an authorization using forms as specified from time to time by the Minister and is supported with the documentation specified in Regulation 8 (4) and where relevant, the documentation specified in Regulation 8 (6) (b), the authorization shall be renewed where the Minister has verified that the requirements of Regulation 13 (1) are still satisfied. Renewal shall be granted for the period necessary for such verification, where an application for such renewal has been made.

(2) Where an application is made for the renewal of an extension of the field of application of an authorization using forms as specified from time to time by the Minister and is supported with the documentation specified in Regulation 16 (2) (a), an extension shall be renewed where the Minister has verified that the requirements of Regulation 16 (2) are still satisfied. Renewal shall be granted for the period necessary for such verification, where an application for such renewal has been made.

(3) An authorization may be reviewed at any time by the Minister and he or she shall require the holder of the authorization concerned, or party to whom an extension of the field of application was granted, to submit further information necessary for completion of the review.

(4) Where an application is made by the holder of an authorization for its modification using a form as determined from time to time by the Minister and is supported with a statement as to the reasons for the proposed modification and with the documentation specified in Regulation 8, an amendment to the authorization may be granted where the Minister has verified that the requirements of Regulation 13 (1), Regulation 15 (2) and Regulation 18 (3), as appropriate, are still satisfied.

(5) Where an application is made by the holder of an authorization for its revocation using a form as determined from time to time by the Minister and is supported with a statement as to the reasons for revocation, the Minister shall revoke the authorization.

(6) Without prejudice to decisions taken pursuant to Regulation 13 (2), the Minister may:

(a) revoke an authorization if he or she is of the opinion that -

(i) the requirements for obtaining the authorization are not, or are no longer, satisfied;
or

(ii) false or misleading particulars were supplied concerning the facts on the basis of which the authorization was granted,
or

(b) modify if it is established that on the basis of developments in scientific and technical knowledge the manner of use and amounts used can be modified.

(7) Following the evaluation of a dossier referred to in Article 6 (3) of the Directive of 1991, the Minister shall, within 6 months -

(a) where it has been decided that the active substance does not satisfy the requirements specified in Article 5 (1) of the Directive of 1991, cancel any authorization granted in accordance with Regulations 13 or 15 (2) for plant protection products containing the active substance, and

(b) where it has been decided to include the active substance in Annex I of the Directive of 1991, modify any authorization granted in accordance with Regulations 13 or 15 (2) and modify any extension of the field of application of any authorization granted in accordance with Regulation 16, for each plant protection product containing the active substance, such that the conditions and restrictions associated with inclusion of the active substance in Annex I of the Directive are complied with.

(8) If the Minister has reason to consider that a plant protection product has been authorized under Regulation 13 (1) or (2) or Regulation 15 (2), constitutes a risk to human or animal health or the environment, he or she shall provisionally restrict or prohibit the use and/or sale of that product and immediately inform the Commission and the other Member States of the action and the reasons for the action.

(9) Following the adoption of a reduced maximum residue level or the adoption of a maximum residue level at or about the limit of quantification for the residue concerned, the Minister shall where necessary modify or revoke authorizations, extensions of the field of application, permissions to market, or notifications granted under these Regulations, or clearances, permissions to market, or notifications granted under the Regulations of 2001, to ensure that the approved uses for relevant products are encompassed by the uses considered for the establishment of any such maximum residue level.

(10) If an authorization is revoked under this Regulation, the Minister shall immediately inform the holder of the authorization of its revocation.

(11) The Minister may grant a period for the disposal, storage, placing on the market and use of existing stocks.

Emergency authorization

20 Notwithstanding Regulations 13, 15 and 18, the Minister may authorize for a period not exceeding 120 days the placing on the market of a plant protection product not complying with those Regulations for limited and controlled use if, in his or her opinion, it is necessary because of an unforeseeable danger that cannot be contained by other means;

Information exchange

21 The Minister shall draw up an annual list of the plant protection products authorized in the State.

Packaging

22. (1) The packaging of a plant protection product together with a fastening or container used in the packaging shall -

(a) be designed and constructed so that its contents cannot escape,

(b) not be susceptible to adverse attack by the contents,

(c) not be liable to form dangerous compounds with the contents,

(d) be strong and solid throughout to resist loosening and meet the normal stresses and strains of handling, and

(e) in the case of a container fitted with replaceable fastening devices, be designed so that the packaging can be refastened repeatedly without the contents escaping.

(2) The packaging of a plant protection product shall not have -

(a) either a shape or graphic decoration likely to attract or arouse the active curiosity of children or mislead consumers, or

(b) a presentation or a designation used for foodstuffs, animal feedingstuffs, medicinal products or cosmetic products.

(3) The packaging of any plant protection product that is placed on the market shall –

(a) be fitted with a child-resistant fastening conforming with the technical specifications provided in Part (A) of Annex IV to the Directive of 1999, and

(b) carry a tactile warning of danger conforming to the technical specifications provided in Part B of Annex IV to the Directive of 1999,

where the criteria specified in Annex IV to the Directive of 1999 taking account of the technical specifications comprising Annex IX to Directive of 1967 as amended by the Directive of 1992 and adapted by Commission Directives 91/410/EEC and 2000/32/EC) are satisfied or where although not dangerous it may nevertheless present a specific hazard.

(4) A package containing a plant protection product shall be closed with a distinctive seal in such a way that when the package is opened for the first time the seal is irreparably damaged.

(5) Where the packaging of a plant protection product includes an inner liner, except where the liner is used as a seal to protect rodenticidal baits, or is a water soluble sachet contained in a sealed foil sachet, it shall not be detachable from the rest of the packaging unless it complies with paragraph (1).

(6) Subparagraphs (a), (b) (c) and (d) of paragraph (1) shall be satisfied if the packaging of a plant protection product complies with the requirements for carriage of dangerous goods by rail, road, inland waterway, sea or air.

Labelling

23. The packaging of a plant protection product or label attached to the packaging, shall comply with the Schedule.

Trials authorizations

24. (1) A person shall not place a plant protection product on the market for use in experiment or tests or use the product in experiments and tests, other than under a trials authorisation where -

(a) the testing or experimentation is for research or development purposes, and

(b) the tests or experiments concerned involve any release into the environment of an
   i. unauthorized plant protection product, or
   ii. authorized plant protection product for an unauthorized use, and

the experiments and tests are carried out in a manner as the Minister may require from time to time

(2) This Regulation, in relation to authorization of plant protection products for trials purposes, shall not apply to experiments or tests covered by Part B of Council Directive No. 90/220/EEC of 23 April 1990 [35].

(3) An application for a trials authorization shall be made in a form as set out from time to time by the Minister and shall be made by or on behalf of the person responsible for, or on whose behalf, the research and development is to be conducted, subject to the person concerned being established in a Member State.

[35] O.J. No. L117/15 8/5/1990

(4) An application for a trials authorization shall be submitted to the Minister at least 45 days before the date on which it is intended that the trial commence and shall be supported with a dossier containing such information as the Minister may from time to time require.

(5) The tests and analyses conducted for the purposes of compiling dossiers referred to in paragraph (4), shall be carried out under agricultural, plant health and environmental conditions relevant to use of the plant protection product in question and representative of those prevailing where the product is intended to be used, and where relevant, shall be officially recognized tests and analyses where they are carried out in the State.

(6) Notwithstanding paragraph (5) and subject to Regulation 10 an applicant need not supply the information relevant to the active substance, except for that identifying the active substance, if -

(a) it is listed in Annex I to the Directive of 1991,

(b) a plant protection product containing the active substance is authorized for a provisional period under Regulation 15,

(c) a plant protection product containing the active substance is authorized under Regulation 18, or

(d) a plant protection product containing the active substance has been granted a clearance under the Regulations of 2001.

(7) The Minister shall examine every application received for a trials authorization and shall decide thereon.

(8) The Minister shall not authorize the placing on the market and use of any plant protection product for trials purposes unless it is satisfied that when used in accordance with the conditions and restrictions specified in paragraphs (10) and (11), it has no harmful effect on human or animal health and no unacceptable influence on the environment.

(9) Restrictions on use, necessary in order to avoid harmful effects on human or animal health that may arise -

(a) through exposure of consumers of treated products to risks of dietary contamination -

(i) in excess of the Acute Reference Dose (ArfD) of the residues concerned,

(ii) in excess of the Acceptable Daily Intake (ADI) level of the residues concerned, or

(iii) due to residues for which the health risks associated with exposure have yet to be established,

(b) through direct exposure of workers and other persons –

(i) in excess of the Acceptable Operator Exposure Level (AOEL) for the active substance concerned, or

(ii) due to exposure to an active substance for which the health risks associated with exposure have yet to be established,

shall, where appropriate, be attached to a trials authorization.

(10) In granting a trials authorization the Minister shall attach any further conditions to the authorization as are necessary and relevant to avoid any harmful effect on human, animal health or the environment, to include -

(a) particular packaging and labelling requirements,

(b) restrictions as to the quantity that may be placed on the market and used for trials purposes,

(c) restrictions as to the area or areas that may be treated, and

(d) conditions necessary to ensure that the use for trials purposes is controlled and subject to official supervision.

(11) A trials authorization -

(a) shall be valid for of 12 months,

(b) may be varied as to any conditions and restrictions attached, where application for such variation is made using forms as determined from time to time by the Minister, and the Minister is satisfied that the provisions of paragraph (9) shall be complied with under the changed conditions or restrictions, and

(c) may be renewed for further fixed periods of 12 months, where application for renewal is made in a form as set out from time to time the Minister.

(12) Experiments and tests conducted in accordance with the conditions and restrictions set out in the trials authorization shall be considered to have been conducted by officially recognized testing facilities or organizations, for the purposes of these Regulations.

(13) Regulations 6, 7, 8, 12, 13, 15, 16 and 18 do not apply to a plant protection product authorized for trial purposes under this Regulation.

Trials permits

25 (1) Subject to paragraph (2), and notwithstanding Regulation 24, the Minister may grant a trials permit to a person involved in research and development, for a particular premises to conduct tests and experiments using plant protection products for which for which a trials authorization has not been granted, or for the use of an authorized plant protection products in a manner not yet authorized, where -

(a) application is made by the person using forms as determined from time to time by the Minister, and

(b) the Minister is satisfied that the requirements specified in paragraph (3) are satisfied.

(2) A person that holds a trials permit is exempt from (6), where they are conducted in accordance with the conditions and restrictions of the trials permit specified pursuant to paragraphs (4) and (5).

(3) A trials permit shall not be granted for particular premises or sites, unless the applicant -

(a) owns, or has exclusive control of premises or sites suitable for conducting trials and experiments,

(b) owns, or has available, equipment and other facilities, necessary for conducting trials and experiments, at each such premises or site, and

(c) holds, or an employee of his or hers holds, appropriate professional qualifications.

(4) Each trials permit granted shall be subject to the condition that -

(a) tests and experiments conducted in accordance with the trials permit shall be carried out as required from time to time by the Minister,

(b) unless the tests and experiments are conducted by an organization or laboratory accredited in accordance with European Standards EN 45002 and EN 45003 to carry out such tests and experiments in accordance with European Standard EN 45001.

(5) Each trials permit granted shall be subject to conditions and restrictions such that the use of plant protection products in tests and experiments conducted in accordance with the trials permit has no harmful effect on human or animal health and no unacceptable influence on the environment including:

(a) restrict its validity to the premises stated in the trials permit,

(b) restrict its validity to tests and experiments conducted under the direct supervision of the professionally qualified personnel referred to in the trials permit, and

(c) being conditional on an authorization for trials purposes being obtained, in each instance in which trials or experiments other than those conforming to the requirements of paragraph (6) are to be conducted.

(6) A trials permits shall not be valid for tests and experiments involving plant protection products unless -

(a) the conditions and manner of use are encompassed by an existing authorization for a plant protection product containing the same active substance or substances,

(b) use is restricted to crops other than food or feed crops,

(c) the nature of the use or of the active substance is such that residues at harvest are precluded, or

(d) food, feed and forage crops are destroyed by burning or burying to preclude consumption by humans or animals.

(7) A trials permit -

(a) shall be granted for fixed periods of 12 months,

(b) may be varied as to any conditions and restrictions attached, where application for such variation is made using forms as determined from time to time by the Minister, and the Minister is satisfied that the provisions of paragraph (3) will be complied with under the changed conditions or restrictions,

(c) may be renewed for a further fixed periods of 12 months, where application for such renewal is made using forms as determined from time to time by the Minister, and

(d) revoked by the Minister where a condition or restriction of the trials permit is breached.

(8) Experiments and tests conducted in accordance with the conditions and restrictions associated with a trials permit, are hereby deemed to have been conducted by officially recognized testing facilities or organizations, for the purposes of these Regulations.

Notification of imports and exports

26. (1) Subject to paragraph (2), a person shall not import a plant protection product into the State unless three days notice in advance of the intended importation has been received by the Minister in a form as set out from time to time by him or her stating-

(a) the brand name of the plant protection product,

(b) the place at which the plant protection product is to be brought into the State,

(c) the date on which the plant protection product is to be brought into the State,

(d) the number of packs that comprise the consignment,

(e) the pack size (given by reference to volume or weight) of the consignment or, in case the consignment comprises more than one pack size, the pack size (so given) of each such pack, and

(f) the destination to which the plant protection product is consigned or, in lieu thereof, an address at which it may be examined, sampled, tested or inspected pursuant.

(2) The Minister may grant an exemption from paragraph (1) if he or she is satisfied that where, following application, the Minister is satisfied that a plant protection product imported and intended for use within the State, in the first instance following importation will be transferred to nominated warehouse or storage facilities pending distribution and sale to end-users, the Minister may grant an exemption from paragraph (1) if -

(a) the importer has provided the name and address of each premises at which plant protection product will be stored following importation, prior to sale,

and

(b) the importer notifies by 31 January in each year details of all imports during the previous year to the Minister using a form as set out from time to time by him or her.

(3) If a plant protection product is exported from the State, the exporter shall notify by 31 January each year details of the export using a form as set out from time to time by the Minister.

Provisional maximum residue levels

27 The maximum levels of residues of a plant protection are

(a) provisional maximum levels established by the Community in accordance with Article 4 (1) (f) of the Directive of 1991, or

(b) maximum levels established by Directive 76/895/EEC [36], Directive 86/362/EEC [37], Directive 86/363/EEC [38], Directive 90/642/EEC [39], or Directive 91/132/EEC [40] amending Directive 74/63/EEC [41].

Products containing residues

28 (1) A person shall not place on the market any product, if -

(a) that product contains within it or on it a residue of a plant protection product, and

(b) the level of such residue exceeds the maximum specified in relation to the product in accordance with Regulation 28 (1);

and such products shall be referred to as controlled products.

(2) A person who contravenes the provisions of paragraph (1) shall be guilty of an offence.

Appointment of authorized officer

29 (1) The Minister may appoint such and so many persons as he or she thinks fit to be authorized officers for the purpose of these Regulations.

(2) An authorized officer shall be furnished with a certificate of his or her appointment as an authorized officer and when exercising any power conferred on him or her by these Regulations shall, if requested by any person affected, produce the certificate to that person.

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[36] O.J. No. L340/26 9/12/1976

[37] O.J. No. L221/36 7/8/1986

[38] O.J. No. L221/43 7/8/1986

[39] O.J. No. L350/71 14/12/1990

[40] O.J. No. L66/16 13/3/1991

[41] O.J. No. L38/31 11/2/1974

[42] O.J. No. L340/26 9/12/1976

Appointment of designated analyst

30 (1) The Minister may appoint such and so many persons as he or she thinks fit to be designated analysts for the purpose of these Regulations

(2) A designated analyst shall be furnished with a certificate of his or her appointment by the Minister to carry out analyses as required by these Regulations.

Search and inspections

31 (1) Subject to paragraph (2), an authorized officer may for the purpose of insuring that these Regulations are being complied with -

(a) at all reasonable times, enter any premises or a place where he or she has reason to believe there is a plant protection product or a controlled product and inspect the premises or place,

(b) require any person in charge of the premises or place or connected with any equipment or other device at that premises or place to produce to him or her any books, documents or records and in the case of such information in a non-legible form to reproduce it in permanent legible form relating to the plant protection product or controlled product and to give to him or her such information as he or she may reasonably require in relation to the plant protection product or controlled product ,

(c) inspect and take copies of, or take extracts from, any such books, documents or records including in the case of information in a non-legible form a copy of or extract from such information in permanent legible form,

(d) there or at any other place, carry out such examinations, inspections or tests of the plant protection product or controlled product found on the premises or at the place as the officer considers appropriate and, if the officer so thinks fit, remove or have removed any plant protection product or controlled product, equipment or other device and retain it for a reasonable period to facilitate such examination, testing or inspection,

(e) examine any procedure connected with the manufacture, placing on the market, processing, storage, usage or transportation of a plant protection product,

(f) take, without payment, such samples of a plant protection product or of a controlled product or of any other substance as the officer may reasonably require and carry out or have carried out on such samples there or elsewhere such checks, analysis and inspections as he or she considers necessary,

(g) secure for later inspection the premises or place or part of it,

(h) if accompanied by -

(I) a member of the Garda Síochána in uniform, or

(II) an officer of the Revenue Commissioners in uniform authorized by them to exercise powers conferred by the Customs Acts or the statutes which relate to the duties of excise,

stop any vehicle which the authorized officer reasonably suspects to contain any plant protection product or controlled product to which these Regulations apply.

(2) An authorized officer shall not, other than with the consent of the occupier, enter a private dwelling unless he or she has obtained a warrant from the District Court under paragraph (5) authorising such entry.

(3) An authorized officer, where he or she considers it necessary, may be accompanied by a member of the Garda Síochána when performing any powers conferred on an authorized officer by this Regulation.

(4) A member of the Garda Síochána not in uniform, when exercising any such power, shall, if so requested by any person affected, produce evidence in writing that he or she is such a member or officer.

(5) If a judge of the District Court is satisfied, on the sworn information of an authorized officer that there are reasonable grounds for suspecting that there is a plant protection product or controlled product on any premises or at any place or that there is any apparatus or other equipment required by him or her for inspection or tests, under this Regulation held in any premises or at any

place, the judge may issue a warrant authorising an authorized officer, accompanied, if appropriate, by other authorized officers or by a member or members of the Garda Síochána at any time or times within one month from the date of issue of the warrant, on production of the warrant requested, to enter those premises or part of it, if need be by reasonable force, and exercise all or any of the powers conferred on an authorized officer under this Regulation.

(6) A person who without reasonable excuse fails to comply with any request or requirement made by an authorized officer under this Regulation is guilty of an offence.

(7) A person who obstructs or interferes with an authorized officer in the exercise of his or her powers under this Regulation or gives an authorized officer information which is false or misleading is guilty of an offence.

(8) A person guilty of an offence under this Regulation is liable on summary conviction to a fine not exceeding €3,000.

Sampling

32 (1) Where a sample is taken the authorized officer concerned shall take such samples in accordance with

(a) the methods described in the manual on the development and use of the Food and Agriculture Organization of the United Nations Plant Production and Protection Paper 149, Fifth Edition specifications for plant protection products as updated from time to time, and

(b) (i) in accordance with Commission Directive 2002/63/EC of 11 July 2002 [43],

(ii) or the Joint Food and Agriculture Organisation of the United Nations and World Health Organization Food Standards Programme, Codex Alimentarius Commission, recommended method of sampling for the determination of Pesticide Residues (Volume 2a, Codex Alimentarius, , "Pesticide Residues in Food, Methods of Analysis and Sampling" 2nd edition, Rome, 2000), where relevant, and

[43] O.J. No. L187/30 16/7/2002

(iii) in accordance with other internationally accepted procedures.

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(c) divide the sample into 2 or more parts, each of which he or she shall seal and mark,

(d) give one part thereof to a designated analyst for analysis in accordance with paragraph (2),

(e) leave with, or send by registered post to, the person in charge of the plant protection product or controlled product or his or her agent, a second part thereof, and

(f) where there is more than one defendant, leave with, deliver to, or send by registered post to each such defendant, a further part thereof.

(2) Where a designated analyst receives a sample from an authorized officer he or she shall analyse it in accordance with a validated method of analysis.

(3) In any proceedings for an offence under these Regulations -

(a) the result of any test, examination or analysis of, or any report on, a sample taken pursuant to this Regulation shall not be adduced unless, before the proceedings were instituted, one of the parts into which the sample was divided (as required by paragraph (1)) was left with, or sent by registered post to, the defendant or his agent,

(b) evidence of the presence of a plant protection product to which the Regulations apply, in or on equipment used for application of the pesticide, is evidence, until the contrary is proved, of the use of the plant protection product by the owner or person in possession of the equipment,

(c) evidence of the presence of a residue of a plant protection product to which the Regulations apply, in or on agricultural produce, soil, compost, surfaces or other materials which may have been treated with or exposed to the plant protection product, is evidence, until the contrary is proved, of the use of the plant protection product by the owner, occupier or person in possession, as the case may be,

(d) a certificate in a form as set out from time to time by the Minister showing the results of an analysis is sufficient evidence until the contrary is shown of the facts certified to in the certificate in relation to -

(i) the presence in a plant protection product of any active substance, impurity or formulating ingredient, and the level of any such presence, or

(ii) the presence of a residue of a plant protection product and the level of such residues in any controlled product, and

(iii) a document purporting to be such a certificate shall be considered, until the contrary is shown, to be such a certificate,

(4) The presence of a plant protection product or controlled product, to which these Regulations apply, on any premises, including any stores, where the business of marketing such a plant protection product or a controlled product is conducted, is sufficient evidence until the contrary is shown that the plant protection product in question is or was being placed on the market by the owner or the person in possession of the product or substance on such premises.

(5) If any person -

(a) tampers with any plant protection product so as to procure that any sample of it taken pursuant to these Regulations does not correctly represent the plant protection product, or

(b) tampers with any controlled product so as to procure that any sample of it taken pursuant to these Regulations does not correctly represent the product sampled, or

(c) tampers or interferes with any sample taken pursuant to these Regulation,

he or she is guilty of an offence.

Seizure, retention, removal and disposal

33 (1) An authorized officer may by a notice in writing given to the owner or to the person in apparent charge or control of a plant protection product or of a controlled product seize and detain the plant protection product or controlled product.

(2) An authorized officer may, in respect of a plant protection product or a controlled product seized under paragraph (1), -

(a) require things specified in the notice to be done in relation to the plant protection product or the controlled product before an authorized officer releases it, and

(b) in the case of a plant protection product, either -

(i) require the disposal of the plant protection product by the person to whom the notice is given, in a manner specified in the notice and at the expense of the owner, or

(ii) indicate the authorized officer's intention of disposing of the plant protection product at the expense of the owner,

such disposal to be, in either case, such as will prevent the said plant protection product from being placed on the market or used, and

(c) in the case of a controlled product require the disposal of the product by the owner, or person in apparent charge or control of the product, in a manner and within a time specified in the notice and at the expense of the owner, such disposal to be such as will prevent the product being used for human or animal consumption,

and in case a notice given under this paragraph requires specified things to be done in relation to a plant protection product or controlled product, the authorized officer shall retain control of the plant protection product or controlled product to which the notice relates until the requirements of the notice have been complied with.

(3) An authorized officer may destroy or otherwise dispose of any plant protection product or a controlled product seized and detained by him or her under Paragraph (1), with the consent of the owner or person in charge of the product or substance or upon the granting of an order under paragraph (6).

(4) An authorized officer who has seized and detained any product or substance may on giving notice in writing to the owner or person in charge of the product or substance apply to a judge of the District Court in whose district court the product or substance was seized for an order directing that the product or substance be destroyed or otherwise disposed of as being a product or substance which is a danger to human or animal health or the environment.

(5) Where a notice is given under this Regulation, a person shall not, without the consent of the authorized officer by whom the notice was given sell, move, dispose of or otherwise interfere with the plant protection product or controlled product in any way pending compliance with the requirements of the notice.

(6) Any person who is aggrieved by a notice given under paragraph (2), in relation to a plant protection product, which either requires the plant protection product to which it relates to be disposed of or indicates an intention to dispose of such a plant protection product may, not later than the expiration of a period of seven days beginning on the date of the notice, appeal against the notice to the District Court in the District Court District in which the notice has been served.

(7) Disposal of a plant protection product pursuant to a notice given under paragraph (2) shall not take place until -

(a) the period during which an appeal under paragraph (4) may be taken against the notice has expired, or

(b) an appeal under that paragraph is determined or withdrawn.

(8) (a) Where an appeal is made to the District Court under paragraph (4), that court, if it is satisfied that -

(i) the plant protection product to which the relevant notice under this Regulation relates is one to which Regulation 3 applies, and

(ii) if the plant protection product was released, it might be placed on the market or used for purposes not authorized in accordance with these Regulations, and

(iii) there has been a failure to comply with the provisions of these Regulations -

shall order that the plant protection product be disposed of in the manner specified in the notice, or in such other manner as may be specified in the court's order and which, in the opinion of the court, will prevent the plant protection product from being used or placed on the market.

(b) Where an order made by the District Court under this paragraph requires the plant protection product to which it relates to be disposed of by an authorized officer, the cost of such disposal shall be recoverable by the Minister as a simple contract debt in any court of competent jurisdiction from the person who was either the owner or in apparent charge or control of the product at the time of its seizure under this Regulation.

(9) Notwithstanding paragraph (2) and the requirements of these Regulations in relation to plant protection products, the method of disposal specified by the authorized officer in a notice given under paragraph (2) may include its use subject to such conditions as the Minister may specify in order to minimize any unacceptable risk to man, animals or the environment that might arise from such use.

(10) In the case of a notice given under paragraph (2) which indicates an intention to dispose of a plant protection product, the ownership of such a plant protection product shall, in the absence of an appeal by the owner against the notice to the District Court, vest in the Minister on the expiration of a period of 7 days beginning on the date of the notice. In the event of an appeal by the owner against the notice to the District Court, ownership of the plant protection product shall vest in the Minister if the court makes an order under paragraph (6) that requires the plant protection product to be disposed of by an authorized officer.

(11) In the case of a notice under paragraph (2) which requires the disposal at the expense of the owner of a plant protection product which has been seized under this Regulation and where there has been a failure to pay, the cost of such disposal shall be recoverable by the Minister as a simple contract debt in any court of competent jurisdiction from the person who was either the owner or in apparent charge or control of the plant protection product at the time of its seizure under this Regulation.

(12) Where there has been failure to comply with a requirement of a notice given under paragraph (2) with respect to a controlled product, an authorized officer who in pursuance of this Regulation has seized any controlled product may, on giving notice in writing to the owner, or the person in apparent charge or control of such product of his intention to do so, apply to the District Court in the District Court

district in which the notice has been served for an order directing that the controlled product be disposed of (by destruction or otherwise) in a manner, specified in the order, that will prevent its being used for human or animal consumption.

(13) Where an application is made under paragraph (12) to the District Court for an order directing the disposal of a controlled product, the Court, if it is satisfied that -

(i) the controlled product to which the notice relates contains within it or on it a residue of a plant protection product in excess of the maximum specified in relation to that product in accordance with Regulation 27,

(ii) if such product were released, it might be put into circulation contrary to Regulation 28, and

(iii) such product if consumed would constitute a danger to human or animal health,

shall order that the product be disposed of (by destruction or otherwise) in a manner, specified in the order that will prevent its being used for human or animal consumption.

(14) Where an order is made by the District Court under paragraph (12), the order may provide that the controlled product to which it relates be disposed of in the manner specified in the notice given under paragraph (2), or in such other manner as may be specified in the Court's order and which, in the opinion of the Court, will prevent the product being used for human or animal consumption.

(15) Where an order made by the District Court under paragraph (12) requires that a product to which it relates be disposed of by an authorized officer, the cost of disposing of the relevant product pursuant to and in accordance with the order shall be recoverable by the Minister as a simple contract debt in any court of competent jurisdiction from the person who was either the owner, or in apparent charge or control of the product, at the time it was seized.

(16) A judge of the District Court to whom an application is made under paragraph (4) shall, if satisfied that such product or substance does not comply with these Regulations or the Directive of 1991 and is a danger to human or animal health or the environment, order that it be destroyed or otherwise disposed of after such a period , not exceeding 14 days, as may be specified in the order, as being a product or substance which is a danger to human or animal health or to the environment.

(17) In the case of a notice under paragraph (1) requiring specific actions or disposal under paragraph (2), all costs incurred shall be the liability of the owner of a plant protection product or a controlled product and where there has been a failure to pay, the cost of such disposal shall be recoverable by the Minister as a simple contract debt in any court of competent jurisdiction from the person who was either the owner or in apparent charge or control of the plant protection product or or a controlled product at the time of its seizure under these Regulations.

General Offences

34 (1) A person who fails to comply with any Regulation under these Regulations shall be guilty of an offence and shall be liable on summary conviction to a fine not exceeding €3,000, or to imprisonment for a term not exceeding 6 months, or to both.

(2) (a) A person shall not forge or utter knowing it to be forged -

(i) a record purporting to be established and maintained under these Regulation or a document purporting to be an extract therefrom (hereafter in this Regulation referred to as "a forged record"), or

(ii) a dispatch document purporting to be issued or given under this Regulation (hereafter in this Regulation referred to as "a forged document").

(b) A person shall not alter with intent to defraud or deceive, or utter knowing it to be so altered –

(i) a record purporting to be established and maintained under these Regulation or a document purporting to be an extract therefrom (hereafter in these Regulation referred to as "an altered record"), or

(ii) a dispatch document purporting to be issued or given under these Regulation (hereafter in this Regulation referred to as "an altered document").

(c) A person shall not have, without lawful authority, in his or her possession a forged record, forged document, altered record or altered document.

(d) A person, in purported compliance with these Regulations, shall not give information that he or she knows to be false or misleading.

Prosecutions and specific rules of evidence

35. (1) An offence under these Regulations may be prosecuted by the Minister.

(2) In proceedings for an offence under these Regulations evidence that claims have been made that a product -

(a) protects plants or plant products against harmful organisms or prevents the action of such organisms,

(b) influences the life processes of plants, other than as a nutrient, (e.g. growth regulators),

(c) preserves plant products,

(d) destroys undesired plants, or

(e) destroys parts of plants, checks or prevents undesired growth of plants,

shall, until the contrary is shown, be sufficient evidence that it is a plant protection product.

(3) (a) In any proceedings for an offence under these Regulations, the result of any test, examination or analysis of, or any report on, a sample taken shall not be adduced unless, before the proceedings were instituted, one of the parts into which the sample was divided was left with, delivered to, or sent by registered post to the defendant or his or her agent.

(b) In any proceedings for an offence under these Regulations, evidence of the presence of a plant protection product in or on equipment capable of use for application of the pesticide, shall be evidence, until the contrary is proved, of the use of the plant protection product by the owner or person in possession of the equipment.

(c) In any proceedings for an offence under these Regulations, evidence of the presence of a residue of a plant protection product, in or on agricultural produce, in soil or compost or in or on surfaces or other materials which may have been treated with or exposed to the plant protection product, shall be evidence, until the contrary is proved, of the use of the plant protection product by the owner, occupier or person in possession, as the case may be.

(d) In any proceedings for an offence under these Regulations, a certificate showing the results of analysis shall, until the contrary is shown, be sufficient evidence of the facts certified to therein in relation to -

(i) the presence in a plant protection product of any active substance, impurity or formulating ingredient and the level of any such presence, or

(ii) the presence of a residue of a plant protection product and the level of such residues in any controlled product, and

a document purporting to be such a certificate shall be such a certificate.

(e) The presence of a plant protection product on any premises (including any stores), shall, until the contrary is shown, be sufficient evidence that the plant protection product in question is or was being placed on the market or used by the owner and by the occupier of such premises.

Fees

36 (1) An application for authorization of a plant protection product or any other service provided or act done under these Regulations shall be accompanied by such fee or part thereof as the Minister may, from time to time, determine.

(2) (a) The Minister shall not consider an application unless it is accompanied by the appropriate fee.

(b) If the Minister determines that a fee or part of a fee is to be paid on an annual basis, the fee or part thereof shall be paid no later than 1 September in the year on which it falls due.

(3) A fee under this Regulation shall be paid in the manner that the Minister may from time to time determine.

(4) A person shall not place a thing in respect of which a fee is payable on the market unless he or she has paid the appropriate fee or fees.

Reduction in fees

37. (1) A person who makes a claim for a reduction or a refund of fees shall -

(a) produce, at the request of an authorized officer, any records, books or other documents that are in his or her possession or under his or her control which substantiate such a claim, and

(b) permit the authorized officer to inspect and take extracts from such records, books or other documents and give to the authorized officer any information which is within his or her knowledge or under his or her control and which such officer may reasonably require for the purpose of verifying the claim, and

(c) afford to such an officer such facilities and assistance as are reasonably necessary for inspecting the stock of the relevant plant protection product if the authorized officer considers such inspection is necessary for the purpose of verifying the claim.

(2) The Minister may, on application, reduce a fee or refund part of a fee.

(3) An application for reduction or refund of a fee shall be in such form and contain such particulars as the Minister may require.

Revocations

38. The following are revoked -

(1) European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) Regulations 1994 (S.I. No. 139 of 1994),

(2) European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) (Amendment) Regulations 1995 (S.I. No. 200 of 1995),

(3) European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) (Amendment) Regulations 1996 (S.I. No. 159 of 1996),

(4) European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) (Amendment) Regulations 1997 (S.I. No. 290 of 1997),

(5) European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) (Amendment) (Number 2) Regulations 1997 (S.I. No. 466 of 1997),

(6) European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) (Amendment) (No. 4) Regulations 1999 (S.I. No. 461 of 1999),

(7) European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) (Amendment) (No. 2) Regulations 2001 (S.I. No. 141 of 2001), and

(8) European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) (Amendment) (No. 4) Regulations 2001 (S.I. No. 623 of 2001).

Savers

39. (1) An authorized officer appointed under the Regulations mentioned in Regulation 39 and holding office immediately before the commencement of these Regulations continues in office after such commencement as if appointed under these Regulations;

(2) Any authorization, permission to place on the market, trials authorization or trials permit granted under any Regulation mentioned in Regulation 39 and in force immediately before the commencement of these Regulations continues in force after such commencement as if granted under these Regulations.

SCHEDULE

Regulation 23

1 The following shall be stated clearly and in an indelible form on all packaging and on a label on, or attached to, the packaging in the Irish language or in the English language or in both languages -

(1) the phrases and inscriptions set out in Annex V to the Directive of 1999, and

(2) the inscription - "To avoid risks to man and the environment, comply with the instructions for use".

(3) the trade name or designation of the plant protection product,

(4) (a) the name and address of the holder of the authorization or permission to market,

(b) if different, the name and address of the person responsible for the final packaging and labelling or for the final labelling of the plant protection product on the market, and

(c) the registration number allocated by the Minister to the plant protection product,

(5) (a) the name of each active substance as given in the list contained in Annex I to the Directive of 1967, if not included therein, its ISO common name or if an ISO name has not yet been assigned, its chemical designation according to IUPAC rules, and

(b) the amount of each active substance so contained expressed for plant protection products that are –

(i) solids, aerosols, volatile liquids (maximum boiling point 50 °C) or viscous liquids (lower limit 1 Pas at 20 °C), as a percentage by weight,

(ii) for other liquids, as a percentage by weight and in grams per litre at 20 °C,for gases, as a percentage by volume,

(iii) for acids, their amides, esters and salts, on an acid equivalent basis,

(6) the net quantity of plant protection product,

(7) the formulation batch number or some means of identifying it,

(8) the chemical name of each substance present in the preparation, excluding active substances, under the designations listed in Annex I to the Directive of 1967 or under an internationally recognised chemical nomenclature if its designation is not included in that Annex, under the following detailed rules

(a) for preparations classified as very toxic, toxic or harmful under Regulation 9 of the Regulations of 2001 and subject to subparagraph (e), the name of every very toxic, toxic or harmful substance present in concentrations equal to, or greater than, the lowest limit laid down for the substances concerned in Annex I to the Directive of 1967, or failing that in Part B of Annex IX of the Regulations of

(b) for preparations classified as corrosive under Regulation 9 of the Regulations of 2001 and subject to subparagraph (e), the name of every corrosive substance present in concentrations equal to, or greater than, the lowest limit laid down for the substances concerned in Annex I to the Directive of 1967, or failing that in Part B of Annex IX of the Regulations of 2001

(c) subject to subparagraph (e), the name of every substance that has given rise to the classification of the preparation in one or more of the following danger categories as set out in Annex IV of the Directive of 1967-

(i) carcinogen category 1, 2 or 3,

(ii) mutagen category 1, 2 or 3,

(iii) toxic for reproduction category 1, 2 or 3,

(iv) very toxic, toxic or harmful due to non-lethal effects after a single exposure,

(v) toxic or harmful due to severe effects after repeated or prolonged exposure, or

(vi) sensitising,

(d) the name of every substance that has given rise to the classification of the preparation in one or more of the following danger categories, where the name of the substance must be included on the label under subparagraphs (a), (b) or (c) as set out in Annex to the Directive of 1967–

(i) explosive,

(ii) oxidising,

(iii) extremely flammable,

(iv) highly flammable,

(v) flammable

(vi) irritant, or

(vii) dangerous for the environment,

(e) unless more are necessary to identify the substances primarily responsible for the major health hazards that gave rise to the classification and choice of corresponding phrases under subparagraphs (a) to (b), a maximum of four chemical names shall suffice,

(9) (a) subject to subparagraph (b) the danger symbols and indications of the dangers specified in Annex II to the Directive of 1967,

(b) where more than one danger symbol must be assigned to a preparation the obligation to apply the symbol -

i. T shall make use of the symbols C and X optional unless otherwise specified in Annex I to the Directive of 1991 to the Directive of 1991,

ii. C shall make use of the symbol X optional,

iii. E shall make use of the symbols F and O optional,

iv. Xn shall make use of the symbol Xi optional,

(c) the danger symbols shall be printed in black on an orange-yellow background,

(10) (a) subject to subparagraphs (b), (c) and (d), risk phrases selected from those included in Annex III to the Directive of 1967,

(b) unless more are necessary to identify the principal hazards, a maximum of six risk phrases shall suffice to describe the risks, for this purpose, the combined phrases listed in Annex III to the Directive of 1967 shall be regarded as single phrases,

(c) in the case of plant protection products classified dangerous in more than one danger category, the risk phrases selected shall cover all of the principal hazards identified,

(d) the risk phrases “extremely flammable” or “highly flammable” need not be used where they describe an indication of danger, used under paragraph (a),

(11) (a) subject to subparagraph (b), safety phrases selected from those included in Annex IV to the Directive of 1967
(b) unless more are necessary to provide appropriate safety advice, a maximum of six safety phrases shall suffice listed from those included in Annex IV to the Directive of 1967,
(c) where it is physically impossible to include the advice on the label or package itself, the package shall be accompanied by safety advice on the use of the plant protection product,

(12) first-aid information for use in the event of accidental exposure or ingestion,

(13) the nature of any special risks for humans, animals or the environment, by means of standard phrases selected as appropriate from those given in Annex IV to the Directive of 1991,

(14) safety precautions for the protection of humans, animals or the environment, in the form of standard phrases selected as appropriate from those given in Annex V to the Directive of 1991,

(15) the type of action of the plant protection product,

(16) the type of preparation,

(17) the uses for which the plant protection product has been included on the register of plant protection products and any specific agricultural, plant health and environmental conditions under which the product may be used or should not be used;

(18) directions for use and the dose rate, expressed in metric units, for each use,

(19) where necessary, the safety interval for each use between application and -

(a) sowing or planting of the crop to be protected,

(b) sowing or planting of succeeding crops,

(c) access by humans or animals,

(d) harvesting, and

(e) use or consumption,

(20) particulars of possible phytotoxicity, varietal susceptibility and any other direct or indirect adverse side effects on plants or products of plant origin together with the intervals to be observed between application and sowing or planting of a crop or subsequent crops,

(21) if accompanied by a leaflet, the sentence "*Read accompanying instructions before use"*,

(22) directions for safe disposal of the plant protection product and of packaging,

(23) the expiry date relevant to normal conditions of storage where the shelf life of the product is limited to less than two years, and

(24) where relevant, the category of users to which supply is restricted.

2 Notwithstanding paragraph 1, the information specified in paragraph 1 (18), (19) and (20) may be included on a separate leaflet accompanying the package if the space available on the package is too small and the leaflet shall be regarded as part of the label. A label and packaging of a plant protection product shall not bear indications such as "*non-toxic"*, "*harmless"*, or other similar indication.

3 Information to the effect that the plant protection product may be used when bees or other non-target species are active, or when crops or weeds are in flower or other such phrases to protect bees or other non-target species may be given on the label, if the authorization relates explicitly to use during the season for bees or other specified organisms and presents minimal hazard to them.

4 Where the information stated in paragraph 1 appears on a label, the label shall be firmly affixed to one or more surfaces of the packaging so that those particulars can be read horizontally when the package is set down normally.

5 The colour and presentation of each label or packaging where the information specified in paragraph 1 is printed on the package, shall be such that the danger symbol and its background stand out clearly from it.

6 The information stated in paragraph 1 shall stand out clearly from its background and shall be of such size and spacing as to be easily read.

7 Notwithstanding paragraph 1 (10) and (11) where the contents of a package do not exceed 125 millilitres -

(a) in the case of a plant protection product classified as highly flammable, oxidising or irritant, with the exception of a product assigned the phrase R41, or classified as dangerous for the environment and assigned the symbol N, the labelling need not include the relevant risk and safety phrases, and

(b) in the case of a plant protection product classified as flammable, or dangerous for the environment but not assigned the N symbol, the labelling need not include the relevant safety phrases.

8 Notwithstanding paragraph 1, the requirements in relation to the information to be included on packaging or on a label attached to packaging shall be satisfied -

(a) in the case of an outer package containing one or more inner packages, if the outer package is labelled under international rules on the transport of dangerous goods and the inner package or packages are labelled under paragraph 1, and

(b) in the case of a single package -

(i) if such a package is labelled under international rules on the transport of dangerous goods and with paragraph 1 (3), (4), (6), (8), (10) and (11),

(ii) for products classified under Regulation 10 of the Regulations of 2001, paragraph 2 (a) shall apply in relation to the property in question when it has not been so identified on the label, or

(iii) where appropriate, for particular types of packaging such as mobile gas cylinders, the specific requirements referred to in Annex VI to the Directive of 1967 are complied with.

9 Where packaging -

(a) is either too small or is unsuitable to enable all the information required by paragraph 1 to be shown on the container itself or on a label or on attached thereto,

(b) containing a plant protection product classified as being harmful, extremely flammable, highly flammable, flammable, irritant or oxidising and the quantity so contained is small and presents no danger to persons handling the plant protection product or any other person,

(c) containing a plant protection product classified as being dangerous for the environment in such small quantities that there is no reason to fear any danger to the environment, or

(d) containing a plant protection product not mentioned in subparagraph (b) or (c) and the quantity so contained is small and presents no danger to persons handling the plant protection product or any other person,

the labelling required under paragraph 1 shall be in a manner that for the time being stands approved of for the purposes of this paragraph by the Minister and which he or she considers appropriate, subject to the symbols, indications of danger, risk phrases and safety phrases used being those specified under paragraph 1.

GIVEN under my Official Seal,
4th March, 2003.

Joe Walsh
Minister for Agriculture and Food

Explanatory Note

(This note is not part of the instrument and does not purport to be a legal interpretation)

These Regulations which consolidate and replace the European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) Regulations, 1994 to 2001 (S.I. No. 139 of 1994, S.I. No. 200 of 1995, S.I. No. 159 of 1996, S.I. No. 290 of 1997, S.I. No. 466 of 1997, S.I. No. 461 of 1999, S.I. No. 141 of 2001, S.I. No. 623 of 2001), also give effect to Commission Directive 2001/36/EC of 16 May 2001, Commission Directive 2001/103/EC of 28 November 2001, Commission Directive 2002/18/EC of 22 February 2002, Commission Directive 2002/37/EC of 3 May 2002, Commission Directive 2002/48/EC of 30 May 2002, Commission Directive 2002/64/EC of 15 July 2002 and Commission Directive 2002/81/EC of 10 October 2002.

The Regulations specify the data requirements for plant protection products containing micro-organisms and for active substances that are micro-organisms, and include the active substances, 2,4-D, isoproturon, ethofumesate, iprovalicarb, prosulfuron, sulfosulfuron, cinidon-ethyl, cyhalofop butyl, famoxadone, florasulam, metalaxyl-M and picolinafen in Annex I to the Directive of 1991 to the Directive of 1991 (*i.e.* in the list of active substances authorized for use in plant protection products).

The amendments made introduce additional definitions, revise the requirements concerning permissions to market, and those concerning extensions in the field of application of plant protection products, make provision for the granting of authorizations for specified periods, amend the packaging and labelling requirements to provide consistency with the European Communities (Classification, Packaging and Labelling of Plant Protection

Products and Biocide Products) Regulations, 2001 (S.I. No. 624 of 2001), amend the control arrangements specified under the Regulations, and allow for amendments to application and annual fees.

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Guidelines

Appendix 1

Annex I to Directive 91/414/EEC

Active Substances Authorised for Use in Plant Protection Products

General provisions applying to all substances listed in this Annex:

In applying the uniform principles set out in Annex VI, in relation to each substance the conclusions of the review report for each such substance, and in particular in Appendices I and II thereof, as finalised in the Standing Committee on the Food Chain and Animal Health, or prior to its establishment in the Standing Committee on Plant Health, on the date indicated under "specific provisions" for that substance, shall be taken into account.

Review reports (except for confidential information specified in Regulation 11) shall be kept available for consultation by any interested parties or shall be made available to them on specific request made.

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
1	Imazalil CAS No 73790-28-0, 35554-44-0 CIPAC No 335	(±)-1-(β-allyloxy-2,4-dichlorophenylethyl) imidazole or (±)-allyl 1-(2,4-dichlorophenyl)-2-imidazol-1-ylethyl ether	975 g/kg	1.1.1999	31.12.2008	Only use as a fungicide may be authorised. For the following uses the following particular conditions apply: - post harvest fruit, vegetable and potato treatments may only be authorised when an appropriate decontamination system is available or a risk assessment has demonstrated that discharge of treatment solution does not have an unacceptable risk for the environment and in particular for aquatic organisms, - post harvest treatment of potatoes may only be authorised when a risk assessment has demonstrated that discharge of processing waste from treated potatoes does not have an unacceptable risk for aquatic

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
						organisms, and - outdoor foliar uses may only be authorised when a risk assessment has demonstrated that use has no unacceptable effects on human and animal health and the environment. The review report was finalised on 11.7.1997.
2	Azoxystrobin CAS No 131860-33-8 CIPAC No 571	Methyl (E)-2-{2[6-(2-cyanophenoxy) pyrimidin-4-yloxy] phenyl}-3-metho-xyacrylate	930 g/kg (Z isomer max. 25 g/kg)	1.7.1998	1.7.2008	Only use as a fungicide may be authorised. In applying the uniform principles, particular attention must be paid to - potential impact on aquatic organisms and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 22.4.1998.
3	Kresoxim-methyl CAS No 143390-89-0 CIPAC No 568	Methyl (E)-2-methoxyimino-2-[2-(o-tolyloxymethyl) phenyl] acetate	910 g/kg	1.2.1999	31.1.2009	Only use as a fungicide may be authorised. In applying the uniform principles, particular attention should be given to the protection of groundwater under vulnerable conditions. The review report was finalised on 16.10.1998.
4	Spiroxamine CAS No 1181134-30-8 CIPAC No 572	(8-tert-Butyl-1,4-dioxaspiro [4,5] decan-2-ylmethyl)-ethylpropylamine	940 g/kg (dia-stereomers A and B combined)	1.9.1999	1.9.2009	Only use as a fungicide may be authorised. In applying the uniform principles, particular attention must be paid to - operator safety and the conditions of authorisation must include appropriate protective measures, and - potential impact on aquatic organisms and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 12.5.1999.

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
5	Azimsulfuron CAS No 120162-55-2 CIPAC No 584	1-(4,6-dimethoxypyrimidin-2-yl)-3-[1-methyl-4-(2-methyl-2H-tetrazol-5-yl)-pyrazol-5-ylsulfonyl]-urea.	980 g/kg	1.10.1999	1.10.2009	Only use as an herbicide may be authorised. Aerial application may not be authorised. In applying the uniform principles, particular attention must be paid to - potential impact on aquatic organisms and terrestrial non-target plants and where appropriate, risk mitigation measures (*e.g.* in rice cultivation minimum holding periods for water prior to discharge) must be included in the conditions of authorisation. The review report was finalised on 2.7.1999.
6	Fluroxypyr CAS No 69377-81-7 CIPAC No 431	4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic acid	950 g/kg	1.12.2000	31.11.2010	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - additional information to be provided as specified in point 7 of the review report, - protection of groundwater, and - potential impact on aquatic organisms and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The Commission should be informed if the additional trials data and information as outlined in point 7 of the review report were not submitted by 1.12.2000. The review report was finalised on 30.11.1999.

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
7	Metsulfuron-methyl CAS No 74223-64-6 EEC No 441	Methyl-2-(4-methoxy-6-methyl-1,3,5-triazin-2-ylcarbamoyl-sulfamo-yl)benzoate.	960 g/kg	1.7.2001	30.6.2011	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater, and - potential impact on aquatic organisms and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 16.6.2000.
8	Prohexadione-calcium CAS No 127277-53-6 CIPAC No 567	Calcium 3,5-dioxo-4-propionylcyclo hexanecarboxylate	890 g/kg	1.10.2000	1.10.2010	Only use as a plant growth regulator may be authorised. The review report was finalised on 16.6.2000.
9	Triasulfuron CAS No 82097-50-5 CIPAC No 480	1-[2-(2-chloroethoxy) phenylsulfonyl]-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)urea	940 g/kg	1.8.2001	31.7.2011	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater, and potential impact on aquatic organisms and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 13.7.2000.
10	Esfenvalerate CAS No 66230-04-4	(S)-α-Cyano-3-phenoxybenzyl-(S)-2-(4-chlorophenyl)-3-methylbutyrate	830 g/kg	1.8.2001	31.7.2011	Only use as an insecticide may be authorised. In applying the uniform principles, particular attention must be paid to

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
	CIPAC No 481	methylbutyrate				- potential impact on aquatic organisms and non-target arthropods and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 13.7.2000.
11	Bentazone CAS No 25057-89-0 CIPAC No 366	3-isopropyl-(1H)-2,1,3-benzothiadiazin-4-(3H)-one-2,2-dioxide	960 g/kg	1.8.2001	31.7.2011	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention should be paid to the protection of groundwater. The review report was finalised on 13.7.2000.
12	Lambda-cyhalothrin CAS No 91465-08-6 CIPAC No 463	A 1:1 mixture of : (S)-α-cyano-3-phenoxybenzyl (Z)-(1R,3R)-3-(2-chloro-3,3,3-trifluoropro-penyl)-2,2-dimethyl-cyclopropanecarbox-ylate and (R)- α-cyano-3-phenoxybenzyl (Z)-(1S,3S)-3-(2-chloro-3,3,3-trifluoropro-penyl)-2,2-dimethyl-cyclopropanecarbox-ylate	810 g/kg	1.1.2002	31.12.2011	Only use as an insecticide may be authorised. In applying the uniform principles, particular attention must be paid to - operator safety, - potential impact on aquatic organisms and non-target arthropods including bees and the conditions of authorisation must include, where appropriate, risk mitigation measures, and - residues in food and especially the acute effects thereof. The review report was finalised on 19.10.2000.
13	(fenhexamid) CAS No 126833-17-8 CIPAC No 603	N-(2,3-dichloro-4-hydroxyphenyl)-1-methylcyclohexane-carboxamide	≥ 950 g/kg	1.6.2001	31.5.2011	Only use as a fungicide may be authorised. In applying the uniform principles, particular attention must be paid to - potential impact on aquatic organisms and where appropriate, risk mitigation measures must be included in

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
						the conditions of authorisation. The review report was finalised on 19.10.2000.
14	Amitrole CAS No 61-82-5 CIPAC No 90	H-[1,2,4]-triazole-3-ylamine	900 g/kg	1.1.2002	31.12.2011	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of operators, - protection of groundwater in vulnerable areas, in particular with respect to non-crop uses, - potential impact on beneficial arthropods, and - potential impact on birds and wild mammals. Use of amitrole during the breeding season may only be authorised when an appropriate risk assessment has demonstrated that there is no unacceptable impact and when the conditions of authorisation include, where appropriate, risk mitigation measures. The review report was finalised on 12.12.2000.
15	Diquat CAS No 2764-72-9 (ion), 85-00-7 (dibromide) CIPAC No 55	9,10-Dihydro-8a,10a-diazoniaphenanthrene ion (dibromide)	950 g/kg	1.1.2002	31.12.2011	On the basis of information available on 12.12. 2000, only use as a terrestrial herbicide and desiccant may be authorised. Use in aquatic weed control shall not be authorised. In applying the uniform principles, particular attention must be paid to - potential impact on aquatic organisms and where appropriate, risk mitigation measures must be included in the conditions of authorisation, and - operator safety during non-professional use and where appropriate, risk mitigation measures must be included in

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
						the conditions of authorisation. The review report was finalised on 12.12.2000.
16	Pyridate CAS No 55512-33.9 CIPAC No 447	6-Chloro-3-phenyl-pyridazin-4-yl S-octyl thiocarbonate	900 g/kg	1.1.2002	31.12.2011	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater, and - potential impact on aquatic organisms and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 12.12.2000.
17	Thiabendazole CAS No 148-79-8 CIPAC No 323	2-Thiazol-4-yl-1H-benzimidazole	985 g/kg	1.1.2002	31.12.2011	Only use as a fungicide may be authorised. Foliar spray applications shall not be authorised. In applying the uniform principles, particular attention must be paid to - potential impact on aquatic and sediment-dwelling organisms and where appropriate, risk mitigation measures must be included in the conditions of authorisation. Suitable risk mitigation measures (*e.g.* depuration with diatom earth or activated carbon) are required to protect surface waters from unacceptable levels of contamination *via* wastewater. The review report was finalised on 12.12.2000.
18	Paecilomyces fumosoroseus Apopka strain 97, PFR 97 or CG 170, ATCC20874	Not applicable	The absence of secondary metabolites should be checked in	1.7.2001	30.06.2011	Only use as an insecticide may be authorised. Each fermentation broth should be checked by HPLC to ensure that no secondary metabolites are present.

No	Common Name, Identification No	IUPAC Name	Purity [(1)]	Entry into Force	Expiration of Inclusion	Specific Provisions
			each fermentation broth by HPLC			The review report was finalised on 27.4.2001.
19	DPX KE 459 (flupyrsulfuron-methyl) CAS No 1447 40-54-5 CIPAC No 577	2-(4,6-dimethoxy-pyrimidin-2-yl-carbamoylsulfamoyl)-6-trifluromethyl-nicotinate monosodium salt	903 g/kg	1.7.2001	30.6.2011	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater. The review report was finalised on 27.4.2001.
20	Acibenzolar-s-methyl CAS No 135158-54-2 CIPAC No 597	Benzo[1,2,3] thiadiazole-7-carbothioic acid S-methyl ester	970 g/kg	1.11.2001	31.10.2011	Only use as a plant activator may be authorised. The review report was finalised on 29.6.2001.
21	Cyclanilide CAS No 113136-77-9 CIPAC No 586	Not available	960 g/kg	1.11.2001	31.10.2011	Only use as a plant growth regulator may be authorised. The content of the impurity 2,4-dichloroaniline (2,4-DCA) in the active substance as manufactured should be ≤ 1 g/kg. The review report was finalised on 29.6.2001.
22	Ferric phosphate CAS No 10045-86-0 CIPAC No 629	Ferric phosphate	990 g/kg	1.11.2001	31.10.2011	Only use as a molluscicide may be authorised. The review report was finalised on 29.6.2001.
23	Pymetrozine CAS No 123312-89-0 CIPAC No 593	(E)-6-methyl-4-[(pyridin-3-yl-metylene)amino]-4,5-dihydro-2H-[1,2,4]-triazin-3 one	950 g/kg	1.11.2001	31.10.2011	Only use as an insecticide may be authorised. In applying the uniform principles, particular attention must be paid to - potential impact on aquatic organisms. The review report was finalised on 29.6.2001.

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
24	Pyraflufen-ethyl CAS No 129630-19-9 CIPAC No 605	Ethyl-2-chloro-5-(4-chloro-5-difluoro-methoxy-l-mhy-pyrazol-3-yl)-4-fluorophenoxyacetate	956 g/kg	1.11.2001	31.10.2011	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - potential impact on algae and aquatic plants and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 29.6.2001.
25	Glyphosate CAS No 1071-83-6 CIPAC No 284	N-(phosphono-methyl)-glycin	950 g/kg	1.7.2002	30.6.2012	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater in vulnerable areas, in particular with respect to non-crop uses. The review report was finalised on 29.6.2001.
26	Thifensulfuron-methyl CAS No 79277-27-3 CIPAC No 452	Methyl 3-(4-methoxy-6-methyl-1,3,5-triazin-2-ylcarbamoyl-sulfamoyl) thiophene-2-carboxylate	960 g/kg	1.7.2002	30.6.2012	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater, and - potential impact on aquatic plants and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 29.6.2001.

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
27	2,4-D CAS No 94-75-7 CIPAC No 1	(2,4-dichlorophenoxy) acetic acid	960 g/kg	1.10.2002	30.9.2012	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater where authorisation would permit use in regions with vulnerable soil and/or climatic conditions, - dermal absorption, and - potential impact on non-target arthropods and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 2.10.2001.
28	Isoproturon CAS No 34123-59-6 CIPAC No 336	3-(4-isopropylphenyl) -1,1-dimethylurea	970 g/kg	1.1.2003	31.12.2012	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater where authorisation would permit use in regions with vulnerable soil and/or climatic conditions or would permit use at rates higher than those described in the review report, and where appropriate, risk mitigation measures must be included in the conditions of authorisation. - potential impact on aquatic organisms and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 7.12.2001.

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
29	Ethofumesate CAS No 26225-79-6 CIPAC No 223	(±)-2-ethoxy-2,3-dihydro-3,3-dimethyl-benzofuran-5-yl-methanesulfonate	960 g/kg	1.3.2003	28.2.2013	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater where authorisation would permit use in regions with vulnerable soil and/or climatic conditions and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 26.2.2002.
30	Iprovalicarb CA No 140923-17-7 CIPAC No 620	{2-Methyl-1-[1-(4-methylphenyl)ethyl-carbonyl]propyl}-carbamic acid isopropylester	950 g/kg provisional specification	1.7.2002	30.6.2011	Only use as a fungicide may be authorised. In applying the uniform principles, particular attention must be paid to - confirmation of the technical specification of the active substance as manufactured by means of appropriate analytical data. The specification of the test material used in toxicity testing must be compared to this specification and be verified, and - protection of operators. The review report was finalised on 26.2.2002.

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
31	Prosulfuron CAS No 94125-34-5 CIPAC No 579	1-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]-urea	950 g/kg	1.7.2002	30.6.2011	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - potential impact on aquatic plants where application is to be made adjacent to surface waters and where appropriate, risk mitigation measures must be included in the conditions of authorisation, and - protection of groundwater where authorisation would permit use in regions with vulnerable soil and/or climatic conditions and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 26.2.2002.
32	Sulfosulfuron CAS No 141776-32-1 CIPAC No 601	1-(4,6-dimethoxy-pyrimidin-2-yl)-3-[2-ethanesulfonyl-imidazol[1,2-α]-pyridine)sulfonyl]urea	980 g/kg	1.7.2002	30.6.2011	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - potential impact on aquatic plants and algae and where appropriate, risk mitigation measures must be included in the conditions of authorisation, and - protection of groundwater when authorisation would permit use in regions with vulnerable soil and/or climatic conditions. The review report was finalised on 26.2.2002.

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
33	Cinidon-ethyl CAS No 142891-20-1 CIPAC No 598	(Z)-ethyl 2-chloro-3-[2-chloro-5-(cyclohex-1-ene-1,2-dicarbox-imido)phenyl]acrylate	940 g/kg	1.10.2002	30.9.2012	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater when authorisation would permit use in regions with vulnerable soil (*e.g.* soils with neutral or high pH values) and/or climatic conditions, and where appropriate, risk mitigation measures must be included in the conditions of authorisation, and - potential impact on aquatic organisms, and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 19.4.2002.
34	Cyhalofop butyl CAS No 122008-85-9 CIPAC No 596	Butyl-(R)-2-[4(4-cyano-2-fluoro-phenoxy)phenoxy] propionate	950 g/kg	1.10.2002	30.9.2012	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - potential impact of aerial applications on non-target organisms and in particular on aquatic species and where appropriate, risk mitigation measures must be included in the conditions of authorisation, and - potential impact of terrestrial applications on aquatic organisms in paddy fields, and where appropriate, risk mitigation measures must be included in the conditions of authorisation. The review report was finalised on 19.4.2002

No	Common Name, Identification No	IUPAC Name	Purity [1]	Entry into Force	Expiration of Inclusion	Specific Provisions
35	Famoxadone CAS No 131807-57-3 CIPAC No 594	3-anilino-5-methyl-5-(4-phenoxyphenyl)-1,3-oxazolidine-2,4-dione	960 g/kg	1.10.2002	30.9.2012	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - potential impact (chronic effects) of parent compound or metabolites on earthworms, - potential impact on aquatic organisms, and where appropriate, risk mitigation measures must be included in the conditions of authorisation, and - protection of operators. The review report was finalised on 19.4.2002
36	Florasulam CAS No 145701-23-1 CIPAC No 616	2',6',8-Trifluoro-5-methoxy-[1,2,4]-triazolo[1,5-c] pyrimidine-2-sulphonanilide	970 g/kg	1.10.2002	30.9.2012	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater when authorisation would permit use in regions with vulnerable soil and/or climatic conditions, and where appropriate, risk mitigation measures must be included in the conditions of authorisation The review report was finalised on 19.4.2002
37	Metalaxyl-M CAS No 70630-17-0 CIPAC No 580	Methyl(R)-2-{[(2,6-dimethylphenyl)-methoxyacetyl]-amino} propionate	910 g/kg	1.10.2002	30.9.2012	Only use as a fungicide may be authorised. In applying the uniform principles, particular attention must be paid to - protection of groundwater from contamination by the active substance or its degradation products CGA 62826

No	Common Name, Identification No	IUPAC Name	Purity [(1)]	Entry into Force	Expiration of Inclusion	Specific Provisions
						and CGA 108906 when authorisation would permit use in regions with vulnerable soil and/or climatic conditions, and where appropriate, risk mitigation measures must be included in the conditions of authorisation The review report was finalised on 19.4.2002
38	Picolinafen CAS No 137641-05-5 CIPAC No 619	4'-Fluoro-6-[(α,α,α-trifluoro-m-tolyl)oxy] picolinanilide	970 g/kg	1.10.2002	30.9.2012	Only use as an herbicide may be authorised. In applying the uniform principles, particular attention must be paid to - potential impact on aquatic organisms, and where appropriate, risk mitigation measures must be included in the conditions of authorisation, and The review report was finalised on 19.4.2002

(1) Further details on identity and specification of active substances are provided in their review reports.

Appendix 2

Annex II to Directive 91/414/EEC

(Annex II to the Directive of 1991, as amended Commission Directive No 93/71/EEC of 27 July 1993, Commission Directive 94/37/EC of 22 July 1994, Commission Directive 94/79/EC of 21 December 1994, the Corrigendum to Commission Directive 94/79/EEC, Commission Directive 95/35/EC of 14 July 1995, Commission Directive 95/36/EC of 14 July 1995, Commission Directive 96/12/EC of 8 March 1996, Commission Directive 96/46/EC of 16 July 1996, Commission Directive 96/68/EC of 21 October 1996, and Commission Directive 2001/36/EC of 16 May 2001)

REQUIREMENTS FOR THE DOSSIER TO BE SUBMITTED FOR THE INCLUSION OF AN ACTIVE SUBSTANCE IN ANNEX I

INTRODUCTION

The information required shall:

1.1 include a technical dossier supplying the information necessary for evaluating the foreseeable risks, whether immediate or delayed, which the substance may entail for humans, animals and the environment and containing at least the information and results of the studies referred to below;

1.2 where relevant, be generated using test guidelines referred to or described in this Annex, in the case of studies initiated before the adoption of the modification of this Annex, the information shall be generated using suitable internationally or nationally validated test guidelines or, in the absence thereof, test guidelines accepted by the competent authority;

1.3 in the event of a test guideline being inappropriate or not described, or where one than those referred to in this annex has been used, include a justification, which is acceptable to the competent authority for the guideline used;

1.4 include, when required by the competent authority, a full description of test guidelines used, except if they are referred to or described in this Annex, and a full description of any deviations from them including a justification, which is acceptable to the competent authority, for these deviations;

1.5 include a full and unbiased report of the studies conducted as well as a full description of them or a justification, which is acceptable to the competent authority where -

- particular data and information which would not be necessary owing to the nature of the product or its proposed uses, are not provided, or
- it is not scientifically necessary, or technically possible to supply information and data;

and

1.6 where relevant, have been generated in accordance with the requirements of Directive 86/609/EEC [44] of 24 November 1986, on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes.

2.1 Tests and analyses must be conducted in accordance with the principles laid down in Directive 87/18/EEC [45] of 18 December 1986, on the harmonization of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their application for tests on chemical substances, where testing is done to obtain data on the properties and/or safety with respect to human or animal health or the environment.

2.2 Notwithstanding the provisions of point 2.1, tests and analyses started on or before the 31 December 1999 and performed to obtain data on the properties and/or safety with respect to honeybees and beneficial arthropods other than bees, may have been conducted by officially recognized testing facilities or organisations, in accordance with the Principles of Good Experimental Practice laid down in the Sixth Schedule, or in compliance with Irish/European Standard IS/EN 45001, where they are conducted within the territory of the State, and in accordance with the requirements of point 2.2 of the introduction to Annex III, where they are conducted outside the territory of the State.

2.3 Notwithstanding the provisions of point 2.1, supervised residue trials conducted in accordance with the provisions of Section 6, relating to plant protection products containing active substances already on the market prior to 25 July 1993 and started on or before the 31 December 1997, may have been conducted by officially recognized testing facilities or organisations, in accordance with the Principles of Good Experimental Practice laid down in the Sixth Schedule, or in compliance with Irish/European Standard IS/EN 45001, where they are conducted within the territory of the State, and in accordance with the requirements of point 2.2 of the introduction to Annex III, where they are conducted outside the territory of the State.

2.4 Notwithstanding the provisions of point 2.1, for active substances consisting of micro-organisms or viruses, tests and analyses done to obtain data on the properties and/or safety with respect to aspects other than human health, may have been conducted by official or officially recognized testing facilities or organisations in accordance with the Principles of Good Experimental Practice laid down in the **Sixth Schedule**, or in compliance with Irish/European Standard IS/EN 45001, where they are conducted within the territory of the State, and in accordance with the requirements of point 2.2 of the introduction to Annex III, where they are conducted outside the territory of the State.

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[44] O.J. No. L358/1, 18/12/1986

[45] O.J. No. L15/3 17/01/1987

PART A

Chemical Substances

1 **Identity of the active substance**

The information provided must be sufficient to identify with precision each active substance, to define it in terms of its specification and to characterize it as to its nature. The information and data referred to, unless otherwise specified, are required for all active substances.

1.1 ***Applicant (name, address, etc.)***

The name and address of the applicant (permanent community address) must be provided as must the name, position, telephone and telefax number of the appropriate person to contact.

Where, in addition, the applicant has an office, agent or representative in the territory of the State, the name and address of the local office, agent or representative must be provided, as must the name, position, telephone and telefax number of the appropriate person to contact.

1.2 ***Manufacturer (name, address, including location of plant)***

The name and address of the manufacturer or manufacturers of the active substance must be provided as must the name and address of each manufacturing plant in which the active substance is manufactured. A contact point (preferably a central contact point, to include name, telephone and telefax number) must be provided, with a view to providing updating information and responding to queries arising, regarding manufacturing technology, processes and the quality of product (including where relevant, individual batches). Where following inclusion of the active substance in Annex I, there are changes in the location or number of manufacturers, the information required must again be notified to the Commission and the Member States.

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

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

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

The chemical name as given in Annex I to the Directive of 1967, or, if not included in that Directive, in accordance with both IUPAC and CA nomenclature, must be provided.

1.5 ***Manufacturer's development code number(s)***

Code numbers used to identify the active substance and, where available, formulations containing the active substance, during development work, must be reported. For each code

number reported, the material to which it relates, the period for which it was used, and the Member States or other countries in which it was used and is being used, must be stated.

1.6 ***CAS, EEC and CIPAC numbers (if available)***

Chemical Abstracts, EEC (EINECS or ELINCS), and CIPAC numbers, where they exist, must be reported.

1.7 ***Molecular and structural formula, molecular mass***

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

1.8 ***Method of manufacture (synthesis pathway) of the active substances***

The method of manufacturer, in terms of the identity of the starting materials, the chemical pathways involved, and the identity of by-products and impurities present in the final product, must be provided, for each manufacturing plant. Generally process engineering information is not required.

Where the information provided relates to a pilot plant production system, the information required must again be provided once industrial scale production methods and procedures have stabilized.

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

The minimum content in g/kg of pure active substance (excluding inactive isomers) in the manufactured material used for production of formulated products, must be reported.

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

1.10 ***Identity of isomers, impurities and additives (e.g. stabilizers), together with the structural formula and the content expressed as g/kg***

The maximum content in g/kg of inactive isomers as well as the ratio of the content of isomers/diastereo-isomers, where relevant, must be provided. In addition, the maximum content in g/kg of each further component other than additives, including by-products, and impurities, must be provided. In the case of additives the content in g/kg must be provided.

For each component, present in quantities of 1 g/kg or more, the following information, where relevant, must be provided -

- chemical name according to IUPAC and CA nomenclature;
- ISO common name or proposed common name if available;
- CAS number, EEC (EINECS or ELINCS) number, and CIPAC number if available;

- molecular and structural formula;
- molecular mass; and
- maximum content in g/kg.

Where the manufacturing process is such that impurities and by-products which are particularly undesirable because of their toxicological, ecotoxicological or environmental properties could be present in the active substance, the content of each such compound must be determined and reported. In such cases, the analytical methods used and the limits of determination, which must be sufficiently low, for each compound of concern, must be reported. Additionally the following information, where relevant, must be provided -

- chemical name according to IUPAC and CA nomenclature;
- ISO common name or proposed common name if available;
- CAS number, EEC (EINECS or ELINCS) number, and CIPAC number if available;
- molecular and structural formula;
- molecular mass; and
- maximum content in g/kg.

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

Where the information provided does not fully identify a component *viz.* condensates, detailed information on their composition must be provided for each such component.

The trade name of components added to the active substance, prior to manufacture of formulated product, to preserve stability and facilitate ease of handling, where they are used, must also be provided. Additionally the following information, where relevant, must be provided for such additives -

- chemical name according to IUPAC and CA nomenclature;
- ISO common name or proposed common name if available;
- CAS number, EEC (EINECS or ELINCS) number, and CIPAC number if available;
- molecular and structural formula;
- molecular mass; and
- maximum content in g/kg.

For added components, other than active substances and other than impurities resulting from the manufacturing process, the function of the component (additive) must be given -

antifoaming agent	buffer
antifreeze	dispersing agent
binder	stabiliser
other (specify)	

1.11 ***Analytical profile of batches***

Representative samples of the active substance must be analysed for content of pure active substance, inactive isomers, impurities and additives, as appropriate. The analytical results reported must include quantitative data, in terms of g/kg content, for all components present in quantities of more than 1 g/kg and typically should account for at least 98% of the material analysed. The actual content of components that are particularly undesirable because of their toxicological, ecotoxicological or environmental properties, must be determined and reported. Data reported must include the results of the analysis of individual samples and a summary of that data, to show the minimum or maximum and typical content of each relevant component, as appropriate.

Where an active substance is produced in different plants this information must be provided for each of the plants separately.

In addition, where available and relevant, samples of the active substance produced in laboratory scale or pilot production systems, must be analysed, if such material was used in generating toxicological or ecotoxicological data.

2 Physical and chemical properties of the active substance

(i) The information provided, must describe the physical and chemical properties of active substances and together with other relevant information, must serve to characterize them. In particular, the information provided must permit -

- physical, chemical, and technical hazards associated with active substances, to be identified;
- classification of active substance as to hazard;
- appropriate restrictions and conditions to be associated with inclusions in Annex I to be selected; and
- appropriate risk and safety phrases to be specified.

The information and data referred to are required for all active substances, except where otherwise specified.

(ii) The information provided, taken together with that provided for relevant preparations, must permit the physical, chemical and technical hazards associated with preparations, to be identified, permit preparations to be classified, and demonstrate that preparations can be used without unnecessary difficulty, and be such that exposure of man, animals, and the environment is minimized, taking account of manner of use.

(iii) The extent to which active substances for which inclusion in Annex I is sought, comply with relevant FAO specifications, must be stated. Divergences from FAO specifications must be described in detail, and justified.

(iv) In certain specified instances, tests must be conducted using purified active substance of stated specification. In such cases the principles of the method(s) of purification used must be reported. The purity of such test material, which must be as high as can be achieved using the best available technology, must be reported. A reasoned justification must be provided in cases where the degree of purity achieved is less than 980 g/kg.

Such justification must demonstrate that all technically feasible and reasonable possibilities for the production of the pure active substance have been exhausted.

2.1 *Melting point and boiling point*

2.1.1 The melting point or where appropriate the freezing or solidification point of purified active substance must be determined in accordance with EEC Method A 1 and be reported. Measurements should be taken up to 360 °C.

2.1.2 Where appropriate, the boiling point of purified active substances must be determined in accordance with EEC Method A 2 and be reported. Measurements should be taken up to 360 °C.

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

2.2 *Relative density*

In the case of active substances that are liquids or solids, the relative density of the purified active substance must be determined in accordance with EEC Method A 3 and be reported.

2.3 ***Vapour pressure (in Pa), volatility (e.g. Henry's law constant)***

2.3.1 The vapour pressure of purified active substance must be determined in accordance with EEC Method A 4 and be reported. Where vapour pressure is less than 10^{-5} Pa, the vapour pressure at 20 or 25 °C may be estimated using a vapour pressure curve.

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

2.4 ***Appearances (physical state, colour and odour; if known)***

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

2.4.2 A description of any odour associated with the active substance as manufactured and with the purified active substance, noted when handling the materials in laboratories or production plants, must be reported.

2.5 ***Spectra (UV/VIS, IR, NMR, MS), molecular extinction at relevant wavelengths***

2.5.1 The following spectra including a table of signal characteristics needed for interpretation must be determined and reported: Ultraviolet/Visible (UV/VIS), infrared (IR), nuclear magnetic resonance (NMR), and mass spectra (MS) of purified active substance. Molecular extinction at relevant wavelengths, must be determined and reported.

The wavelengths at which UV/visible molecular extinction occurs are to be determined and reported and must include, where appropriate, a wavelength at the highest absorption value above 290 nm.

In the case of active substances that are resolved optical isomers their optical purity must be measured and reported.

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

2.6 ***Solubility in water including effect of pH (4 to 10) on solubility***

The water solubility of purified active substances under atmospheric pressure must be determined in accordance with EEC Method A 6 and be reported. These water solubility determinations must be made in the neutral range (*i.e.* in distilled water in equilibrium with atmospheric carbon dioxide). Where the active substance is capable of forming ions, determinations must also be made in the acidic range (pH 4 to 6) and in the alkaline range (pH 8 to 10), and be reported. Where the stability of the active substances in aqueous media is such that water solubility cannot be determined, a justification based on test data must be provided.

2.7 ***Solubility in organic solvents***

The solubility of active substances, as manufactured, in the following organic solvents at 15 to 25 °C must be determined and reported if less than 250 g/kg; the temperature applied must be specified:

aliphatic hydrocarbon	- preferably n-heptane
aromatic hydrocarbon	- preferably xylene
halogenated hydrocarbon	- preferably 1,2-dichlorethane
alcohol	- preferably methanol or isopropyl acetone
ketone	- preferably acetone
ester	- preferably ethyl acetate

If for a particular active substance, one or more of these solvents is unsuitable (*e.g.* reacts with test material), alternative solvents can be used instead. In such cases, choices made must be justified in terms of their structure and polarity.

2.8 ***Partition co-efficient n-octanol/water including effect of pH (4 to 10)***

The n-octanol/water partition coefficient of purified active substance must be determined in accordance with EEC Method A 8 and be reported. The effect of pH (4 to 10) must be investigated when the substance is acidic or basic as defined by its pKa value (< 12 for acids, > 2 for bases).

2.9 ***Stability in water, hydrolysis rate, photochemical degradation, quantum yield and identity of breakdown product(s), dissociation constant including effect of pH (4 to 9)***

2.9.1 The hydrolysis rate of purified active substances (usually radiolabelled active substance, > 95% purity), for each of the pH values 4, 7 and 9, under sterile conditions, in the absence of light, must be determined in accordance with EEC Method C 7 and be reported. For substances with a low rate of hydrolysis, the rate can be determined at 50 °C, or another appropriate temperature.

If degradation is observed at 50 °C, degradation rate at another temperature must be determined, and an Arrhenius plot must be constructed to permit an estimate to be made of hydrolysis at 20 °C. The identity of hydrolysis products formed and the rate constant observed, must be reported. The estimated DT_{50} value must also be reported.

2.9.2 For compounds with a molar (decadic) absorption coefficient (ε) > 10 (1 x mol^{-1} x cm^{-1}) at a wavelength λ ≥ 290 nm, direct phototransformation in purified (*e.g.* distilled) water at 20 to 25 °C, of purified active substance usually radio labelled using artificial light under sterile conditions, if necessary using a solubilizer, must be determined and reported. Sensitizers such as acetone must not be used as a co-solvent or solubilizer. The light source must simulate sunlight and be equipped with filters to exclude radiation at wavelengths λ < 290 nm. The identity of breakdown products formed which at any time during the study are present in quantities ≥ 10% of the active substance added, a mass balance to account for at least 90% of the applied radioactivity, as well as photochemical half-life must be reported.

2.9.3 Where necessary to investigate direct phototransformation, the *quantum yield of direct photodegradation in water* must be determined and reported, together with calculations to estimate theoretical lifetime of the active substance in the top layer of aqueous systems and the real lifetime of the substance.

The methodology to be used is that described by SETAC [46].

2.9.4 Where dissociation in water occurs, the dissociation constant(s) (pKa values) of purified active substances must be determined in accordance with OECD Test Guideline 112 and be reported. The identity of the dissociated species formed, based on theoretical considerations, must be reported. If the active substance is a salt, the pKa value of the active principle must be given.

2.10 ***Stability in air, photochemical degradation, identity of breakdown product(s)***

An estimation of the photochemical oxidative degradation (indirect phototransformation) of the active substance(s), must be submitted.

2.11 ***Flammability including auto-flammability***

2.11.1 The flammability of active substances as manufactured, which are solids, gases, or are substances which evolve highly flammable gases, must be determined in accordance with EEC Methods A 10, A 11 or A 12, as appropriate, and be reported.

2.11.2 The auto-flammability of active substances as manufactured must be determined in accordance with EEC Method A 15 or A 16, as appropriate, and/or, where necessary, according to the UN-Bowes-Cameron-Cage-Test (UN-Recommendations on the Transport of Dangerous Goods, Chapter 14, Nr. 14.3.4), and be reported.

[46] Society of Environmental Toxicology and Chemistry (SETAC), 1995, "Procedures for assessing the environmental fate and ecotoxicity of pesticides, ISBN 90-5607-002-9"

2.12 ***Flash point***

The flash point of active substances as manufactured with a melting point below 40 °C, must be determined in accordance with EEC Method A 9 and be reported; only closed cup methods should be used.

2.13 ***Explosive properties***

The explosive properties of active substances as manufactured, must be determined in accordance with EEC Method A 14, where appropriate, and be reported.

2.14 ***Surface tension***

The surface tension of active substances must be determined in accordance EEC Method A 5 and be reported.

2.15 ***Oxidizing properties***

The oxidizing properties of active substances as manufactured, must be determined in accordance with EEC Method A 17 and be reported, except where examination of their structural formulae, establishes beyond reasonable doubt that the active substance concerned is incapable of reacting exothermically with a combustible material. In such cases, it is sufficient to provide that information as justification for not determining the oxidizing properties of the substance.

3 **Further information on the active substance**

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

(ii) The information provided must specify the normal methods and precautions to be followed, in the handling, storage and transport of the active substance.

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

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

(v) The information and data referred to are required for all active substances, except where otherwise specified.

3.1 ***Function, e.g. fungicide, herbicide, insecticide, repellent, growth regulator***

The function must be specified from among the following:

acaricide	molluscicide	semio-chemicals
bactericide	nematicide	talpicide
fungicide	plant growth regulator	viricide
herbicide	repellent	other (must be specified)
insecticide	rodenticide	

3.2 ***Effects on harmful organisms, e.g. contact poison, inhalation poison, stomach poison, fungitoxic or fungistatic, etc. systemic or not in plants***

3.2.1 The nature of the effects on harmful organisms must be stated:

contact action	fungitoxic action	reproduction inhibitor
stomach action	fungistatic action	other (must be specified)
inhalation actiondesiccant		

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

3.3 ***Field of use envisaged, e.g. field, protected crops, storage of plant products, home gardening***

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

Field use
- Agriculture
- Horticulture
- Forestry
- Viticulture

Protected crops

Amenity

Weed control on non-cultivated areas

Home gardening

Houseplants

Plant products storage practice

Other (specify)

3.4 ***Harmful organisms controlled and crops or products protected or treated***

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

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

3.4.3 Where relevant, effects achieved *e.g.* sprout suppression, retardation of ripening, reduction in stem length, enhanced fertilization etc., must be reported.

3.5 ***Mode of action***

3.5.1 To the extent that it has been elucidated, a statement must be provided as to the mode of action of the active substance in terms, where relevant, of the biochemical and physiological mechanism(s) and biochemical pathway(s) involved. Where available, the results of relevant experimental studies must be reported.

3.5.2 Where it is known that to exert its intended effect, the active substance must be converted to a metabolite or degradation product following application or use of preparations containing it, the following information, cross referenced to and drawing on information provided in the context of paragraphs 5.1, 5.10, 6.1, 6.2, 6.7, 7.1, 7.2 and 9, where relevant, must be provided for the active metabolite or degradation product -

- chemical name according to IUPAC and CA nomenclature;
- ISO common name or proposed common name;
- CAS number, EEC (EINECS or ELINCS) number, and CIPAC number if available;
- empirical and structural formula; and
- molecular mass.

3.5.3 Available information relating to the formation of active metabolites and degradation products, must be provided, to include -

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

3.6 ***Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies***

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

3.7 ***Recommended methods and precautions concerning handling, storage, transport or fire***

A Safety Data Sheet prepared in accordance with the provisions of Article 27 of the Directive of 1967 must be provided for all active substances.

3.8 ***Procedures for destruction or decontamination***

3.8.1 Controlled incineration

In many cases the preferred or sole means to safely dispose of active substances, contaminated materials, or contaminated packaging, is through controlled incineration in a licensed incinerator.

Where the content of halogens of the active substance is greater than 60 %, the pyrolytic behaviour of the active substance under controlled conditions (including, where relevant, supply of oxygen and residence time), at 800 °C and the content of polyhalogenated dibenzo-p-dioxins and dibenzo-furans in the products of pyrolysis must be reported. The applicant must provide detailed instructions for safe disposal.

3.8.2 Others

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

3.9 ***Emergence measures in case of an accident***

Procedures for the decontamination of water in case of an accident must be provided.

4 **Analytical methods**

Introduction

(i) The provisions of this section only cover analytical methods required for post- registration control and monitoring purposes.

(ii) For analytical methods used for the generation of data as required in accordance with Annex HA, or for other purposes, applicants must provide a justification for the method used; where

necessary separate guidance will be developed for such methods on the basis of the requirements defined for methods for post-registration control and monitoring purposes.

(iii) Descriptions of methods must be provided and include details of equipment, materials and conditions used.

(iv) As far as practicable methods provided must employ the simplest approach, involve the minimum cost, and require commonly available equipment.

(v) For the purposes of this section, the following definitions apply:

impurities	any component other than the pure active substance that is present in the active substance as manufactured (including non- active isomers) originating from the manufacturing process or from degradation during storage;
relevant impurities	impurities of toxicological and/or ecotoxicological or environmental concern;
significant impurities	impurities with a content of ≥ I g/kg in the active substance as manufactured;
metabolites	metabolites include products resulting from degradation or reaction of the active substance;
relevant metabolites	metabolites of toxicological and/or ecotoxicological or environmental concern.

On request the following samples must be provided:

- analytical standards of the pure active substance,
- samples of the active substance as manufactured,
- analytical standards of relevant metabolites and all other components included in the residue definition,
- if available, samples of reference substances for relevant impurities.

4.1 ***Methods for the analysis of the active substance as manufactured***

For point 4.1 the following definitions apply:

(i) *Specificity*

Specificity is the ability of a method to distinguish between the analyte being measured and other substances

(ii) *Linearity*

Linearity is defined as the ability of the method, within a given range, to obtain an acceptable linear correlation between the results and the concentration of analyte in samples.

(iii) *Accuracy*

The accuracy of a method is defined as the degree to which the determined value of analyte in a sample corresponds to the accepted reference value (*e.g.* ISO 5725).

(iv) *Precision*

Precision is defined as the closeness of agreement between independent test results obtained under prescribed conditions.

Repeatability: Precision under repeatability conditions, *i.e*. conditions where independent test results are obtained with the same method on identical test material in the same laboratory by the same operator using the same equipment within short intervals of time.

Reproducibility need not be determined for the active substance as manufactured (for definition of reproducibility see ISO 5725).

4.1.1 Methods, which must be described in full, must be provided for the determination of pure active substance in the active substance as manufactured as specified in the dossier submitted in support of inclusion in Annex 1. The applicability of existing CIPAC methods must be reported

4.1.2 Methods must also be provided for the determination of significant and/or relevant impurities and additives (*e.g.* stabilizers) in the active substance as manufactured.

4.1.3 *Specificity, linearity, accuracy and repeatability*

4.1.3.1 Specificity of methods submitted, must be demonstrated and reported. In addition the extent of interference by other substances present in the active substance as manufactured (*e.g.* isomers, impurities or additives), must be determined.

While interferences due to other components may be identified as systematic errors, in the assessment of the accuracy of methods proposed for the determination of pure active substance in the active substance as manufactured, an explanation must be provided for any interference occurring which contributes more than ± 3% to the total quantity determined. The degree of interference for methods for the determination of impurities must also be demonstrated.

4.1.3.2 The linearity of proposed methods over an appropriate range, must be determined and reported. For the determination of pure active substance, the calibration range must extend (by at least 20 %) the highest and lowest nominal content of the analyte in relevant analytical solutions. Duplicate calibration determinations must be made at 3 or more concentrations. Alternatively, 5 concentrations, each as single measurements, are acceptable. Reports submitted must include the equation of the calibration line and the correlation co-efficient and representative and properly labelled documentation from the analysis, *e.g.* chromatograms.

4.1.3.3 Accuracy is required for methods for the determination of pure active substance and significant and/or relevant impurities in the active substance as manufactured.

4.1.3.4 To determine repeatability with respect to the analysis of the pure active substance, a minimum of five determinations must, in principle, be made. The relative standard deviation (% RSD) must be reported. Outliers identified through an appropriate method (*e.g.* Dixon's or Grubb's Test), may be discarded. Where outliers have been discarded, that fact must be clearly indicated. An explanation as to the reason for the occurrence of individual outliers, must be attempted.

4.2 ***Methods for the determination of residues***

The methods reported must be capable of determining the active substance and where relevant metabolites. For each method and for each relevant representative matrix, the specificity, precision, recovery, and limit of determination must be experimentally determined and be reported.

In principle, residue methods proposed should be multi-residue methods; a standard multi-residue method must be assessed and reported as to its suitability for residue determination. Where residue methods proposed are not multi-residue methods, or are not compatible with such methods, an alternative method must be proposed. Where this requirement results in an excessive number of methods for individual pesticides, a 'common moiety method' may be acceptable.

For this section the following definitions apply

(i) *Specificity*

Specificity is the ability of a method to distinguish between the analyte being measured and other substances

(ii) *Precision*

Precision is defined as the closeness of agreement between independent test results obtained under prescribed conditions.
Repeatability: Precision under repeatability conditions, *i.e.* conditions where independent test results are obtained with the same method on identical test material in the same laboratory by the same operator using the same equipment within short intervals of time.

Reproducibility: As reproducibility as generally defined (*e.g.* in ISO 5725) is generally not practicable for residue analytical methods, reproducibility in the context of this Annex is defined as a validation of the repeatability of recovery, from representative matrices, at representative levels, by at least one laboratory which is independent from that which initially validated the study (this independent laboratory may be within the same company) (independent laboratory validation).

(iii) *Recovery*

The percentage determinable of the amount of active substance or relevant metabolite added to a sample of the appropriate matrix that previously contained no detectable level of the analyte.

(iv) *Limit of determination*

The limit of determination (often referred to as limit of quantification) is defined as the lowest concentration tested, at which an acceptable mean recovery is obtained (normally 70-110% with a relative standard deviation of preferably ≤ 20%; in certain justified cases lower or higher mean recovery rates as well as higher relative standard deviations may be acceptable).

4.2.1 *Residues in and/or on plants, plant products, foodstuffs (of plant and animal origin), feedingstuffs*

Methods submitted must be suitable for the determination of all components included in the residue definition, as submitted in accordance with provisions of point 6.1 and 6.2 of this Annex, in order to enable Member States to monitor compliance with established MRLs or to determine dislodgeable residues.

The specificity of the methods proposed must enable all components included in the residue definition to be determined, using an additional confirmatory method if appropriate.

The repeatability of methods proposed must be determined and reported. Replicate analytical portions for testing can be prepared from a common field treated sample, containing incurred residues. Alternatively the replicate analytical portions can be prepared from a common untreated sample with aliquots fortified at the required level(s).

The results from an independent laboratory validation must be reported.

The limit of determination including the individual and mean recovery levels obtained must be determined and reported. The overall relative standard deviation, as well as the relative standard deviation for each fortification level must be experimentally determined and be reported.

4.2.2 *Residues in soil*

Methods for analysis of soil for parent compound and/or relevant metabolites must be submitted.

The specificity of the methods must be such as to enable the parent compound and/or relevant metabolites to be determined, using an additional confirmatory method if appropriate.

The repeatability, recovery and the limit of determination including the individual and mean recovery levels must be determined and reported. The overall relative standard deviation, as well as the relative standard deviation for each fortification level must be experimentally determined and be reported.

The proposed limit of determination must not exceed a concentration that is of concern with regard to exposure of non-target organisms or because of phytotoxic effects. Normally the proposed limit of determination should not exceed 0.05 mg/kg.

4.2.3 *Residues in water (including drinking water, ground water and surface water)*

Methods for analysis of water for parent compound and/or relevant metabolites must be submitted.

The specificity of the methods must be such as to enable the parent compound and/or relevant metabolites to be determined, using an additional confirmatory method if appropriate.

The repeatability, recovery and the limit of determination including the individual and mean recovery levels must be determined and be reported. The overall relative standard deviation, as well as the relative standard deviation for each fortification level must be experimentally determined and be reported.

For drinking water the proposed limit of determination must not exceed 0.1 μg/L. For surface water the proposed limit of determination must not exceed a concentration that has an impact on non-target organisms deemed to be unacceptable according to the requirements of Annex VI.

4.2.4 *Residues in air*

Methods for the analysis of air for the active substance and/or relevant metabolites formed during or shortly after application must be submitted unless it can be justified that exposure of operators, workers or bystanders is not likely to occur.

The specificity of the methods must be such as will enable the parent compound and/or relevant metabolites to be determined, using an additional confirmatory method if appropriate.

The repeatability, recovery and the limit of determination including the individual and mean recovery levels must be determined and be reported. The overall relative standard deviation, as well as the relative standard deviation for each fortification level must be experimentally determined and be reported.

The proposed limit of determination must take into account relevant health based limit values or relevant exposure levels.

4.2.5 *Residues in body fluids and tissues*

Where an active substance is classified as toxic or highly toxic, appropriate analytical methods must be submitted.

The specificity of the methods must enable the parent compound and/or relevant metabolites to be determined, using an additional confirmatory method if appropriate.

The repeatability, recovery and the limit of determination including the individual and mean recovery levels must be determined and be reported. The overall relative standard deviation, as well as the relative standard deviation for each fortification level must be experimentally determined and be reported.

5 **Toxicological and metabolism studies**

Introduction

(i) The information provided, taken together with that provided for one or more preparations containing the active substance, must be sufficient to permit an evaluation to be made as to the risks for man, associated with the handling and use of plant protection products containing the active substance, and the risks for man arising from residual traces remaining in food and water. In addition, the information provided must be sufficient to -

- permit a decision to be made as to whether, or not, the active substance can be included in Annex I,
- specify appropriate conditions or restrictions to be associated with any inclusion in Annex I,
- classify the substance as to hazard,
- establish a relevant acceptable daily intake (ADI) level for man,
- establish acceptable operator exposure level(s) (AOEL),
- specify the hazard symbols, the indications of danger, and the risk and safety phrases for the protection of man, animals and the environment to be included on packaging (containers),
- identify relevant first aid measures as well as appropriate diagnostic and therapeutic measures to be followed in the event of poisoning in man, and
- permit an evaluation to be made as to the nature and extent of the risks for man, animals (species normally fed and kept or consumed by man) and of the risks for other non-target vertebrate species.

(ii) There is no need to investigate and report all potentially adverse effects found during routine toxicological investigations (including effects on organs and special systems such as immunotoxicity and neurotoxicity) and to undertake and report such additional studies which may be necessary to investigate the probable mechanism involved, to establish NOAELs (no observed adverse effect levels), and to assess the significance of these effects. All available biological data and information that are relevant to the assessment of the toxicological profile of the substance tested, must be provided.

(iii) In the context of the influence that impurities can have on toxicological behaviour, it is essential that for each study submitted, a detailed description (specification) of the material used, as mentioned under section 1 point 11, be provided. Tests should be conducted using active substance of that specification to be used in the manufacture of preparations to be authorized, except where radiolabelled material is required or permitted.

(iv) Where studies are conducted using an active substance produced in the laboratory or in a pilot plant production system, the studies must be repeated using the active substance as manufactured, unless it can be justified that the test material used is essentially the same, for the purposes of toxicological testing and assessment. In cases of uncertainty, appropriate bridging studies must be submitted to serve as a basis for a decision as to the possible need for repetition of studies.

(v) In the case of studies in which dosing extends over a period, dosing should preferable be done using a single batch of active substance if stability permits.

(vi) For all studies actual achieved dose in mg/kg body weight, as well as in other convenient units, must be reported. Where dosing via the diet is utilized the test compound must be distributed uniformly in the diet.

(vii) Where, as a result of metabolism or other processes in or on treated plants, or as a result of processing of treated products, the terminal residue (to which consumers or workers as defined in Annex III, point 7.2.3 will be exposed) contains a substance which is not the active substance itself and is not identified as a metabolite in mammals, it will be necessary to carry out toxicity studies on those components of the terminal residue unless it can be demonstrated that consumer or worker exposure to these substances does not constitute a relevant risk to health. Toxicokinetic and metabolism studies relating to metabolites and degradation products should only be conducted if toxicity findings of the metabolite cannot be evaluated by the available results relating to the active substance.

(viii) The route of administration of the test substance depends on the main exposure routes. In cases where exposure is mainly to the gas phase, it can be more appropriate to perform inhalation studies instead of oral studies.

5.1 ***Studies on absorption, distribution, excretion and metabolism in animals***

Quite limited data, as described below and restricted to one test species (normally the rat) may be all that is required. These data can provide information useful in the design and interpretation of subsequent toxicity tests. However, it must be remembered that information on inter species differences may be crucial in extrapolation of animal data to man and information on percutaneous penetration, absorption, distribution, excretion and metabolism may be useful in operator risk assessments. It is not possible to specify detailed data requirements in all areas, since the exact requirements will be dependant upon the results obtained for each particular test substance.

Aim of the test

The tests should provide sufficient data to permit -

- an evaluation of the rate and extent of absorption,
- the tissue distribution and the rate and extent of excretion of the test substance and of relevant metabolites,
- the identification of metabolites and the metabolic pathway.

The effect of dose level on these parameters and whether results are different after single versus repeated doses, should also be investigated.

Circumstances in which required

A single dose toxicokinetic study in rats (oral route of administration) in at least two dose levels as well as a repeated dose toxicokinetic study in rats (oral route of administration) at a single dose level, must be conducted and reported. It may be necessary in some cases to perform additional studies on another species (such as goat or chicken).

Test guideline

Commission Directive 88/302/EEC [47], Part B, Toxicokinetics.

5.2 ***Acute toxicity***

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

- the toxicity of the active substance,
- the time course and characteristics of the effects with full details of behavioural changes and possible gross pathological changes at post-mortem,
- where possible mode of toxic action, and
- the relative hazard associated with the different routes of exposure.

While the emphasis must be on estimating the toxicity ranges involved, the information generated must also permit the active substance to be classified in accordance with the Directive of 1967. The information generated through acute toxicity testing is of particular value in assessing hazards likely to arise in accident situations.

5.2.1 *Oral*

Circumstances in which required

The acute oral toxicity of the active substance must always be reported

Test Guideline

The test must be carried out in accordance with EEC Method B 1 or B 1 bis.

[47] O.J. No. L133/1 30/05/1988

5.2.2 *Percutaneous*

Circumstances in which required

The acute percutaneous toxicity of the active substance must always be reported

Test Guideline

Both local and systemic effects must be investigated. The test must be carried out in accordance with EEC Method B 3.

5.2.3 *Inhalation*

Circumstances in which required

The inhalation toxicity of the active substance must be reported where the active substance is -

- a gas or a liquefied gas,
- to be used as a fumigant,
- to be included in a smoke generating, aerosol or vapour releasing, preparation,
- to be used with fogging equipment,
- has a vapour pressure > 1 x 10^{-2} Pa and is to be included in preparations to be used in enclosed spaces such as warehouses or glasshouses,
- to be included in preparations which are powders containing a significant proportion of particles of diameter < 50 μm (> 1 % on a weight basis), or
- to be included in preparations to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 μm (> 1 % on a weight basis).

Test Guideline

The test must be carried out in accordance with EEC Method B 2.

5.2.4 *Skin irritation*

Aim of the test

The test will provide information as to the potential for skin irritancy of the active substance, including the potential reversibility of the effects observed.

Circumstances in which required

The skin irritancy of the active substance must be determined and reported except where it is likely, as indicated in the test guideline, that severe skin effects may be produced or that effects can be excluded.

Test Guideline

The test must be carried out in accordance with EEC Method B 4.

5.2.5 *Eye irritation*

Aim of the test

The test will provide information as to the potential for eye irritancy of the active substance, including the potential reversibility of the effects observed.

Circumstances in which required

Eye irritation tests must be conducted and reported except where it is likely, as indicated in the test guideline, that severe effects on the eye may be produced.

Test Guideline

The test must be carried out in accordance with EEC Method B 5.

5.2.6 *Skin sensitisation*

Aim of the test

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

Circumstances in which required

The test must always be carried out except where the substance is a known sensitizer.

Test Guideline

The test must be carried out in accordance with EEC Method B 6.

5.3 ***Short-term toxicity***

Short-term toxicity studies must be designed to provide information as to the amount of the active substance that can be tolerated without toxic effects under the conditions of the study. Such studies provide useful data on the risks for those handling and using preparations containing the active substance. In particular, short-term studies provide an essential insight into possible cumulative effects of the active substance and the risks to workers who may be exposed over extensive periods. In addition short-term studies provide information that is useful in the design of chronic toxicity studies.

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

- the relationship between dose and adverse effects,
- the toxicity of the active substance including where possible the NOAEL,
- the target organs, where relevant,
- the time course and characteristics of poisoning with full details of behavioural changes and possible pathological findings at post-mortem,
- specific toxic effects and pathological changes produced,
- where relevant the persistence and reversibility of certain toxic effects observed, following discontinuation of dosing,
- where possible, the mode of toxic action, and
- the relative hazard associated with different routes of exposure.

5.3.1 *Oral 28-day study*

Circumstances in which required

Although it is not mandatory to perform 28-day short-term studies, they can be useful as range finding tests. Where conducted they must be reported, since the results can be of particular value in the identification of adaptive responses which can be masked in chronic toxicity studies.

Test Guideline

The test must be carried out in accordance with EEC Method B 7.

5.3.2 *Oral 90-day study*

Circumstances in which required

The short-term (90 day) of the active substance to both rat and dog, must always be reported. Where there is evidence that the dog is significantly more sensitive and where such data are likely to be of value in extrapolating results obtained to man, a 12-month toxicity study in dogs must be conducted and reported.

Test Guideline

Commission Directive 88/302/EEC, Part B, sub-chronic oral toxicity test.

5.3.3 *Other routes*

Circumstances in which required

For the assessment of the significance of operator exposure, percutaneous studies may be useful.

For volatile substances (vapour pressure > 10^{-2} Pa) expert judgement is required to decide whether the short-term studies have to be performed by the oral inhalation route of exposure.

Test Guidelines

- 28-day dermal: EEC Method B 9,
- 90-day dermal: Commission Directive 88/302/EEC, Part B, sub-chronic dermal toxicity study,
- 28-day inhalation: EEC Method B 8,
- 90-day inhalation: Commission Directive 88/302/EEC, Part B, sub-chronic inhalation toxicity study.

5.4 ***Genotoxicity testing***

Aim of the test

These studies are of value in -

- the prediction of genotoxic potential,
- the early identification of genotoxic carcinogens, and
- the elucidation of the mechanism of action of some carcinogens.

To avoid responses that are artefacts of the test system, excessively toxic doses must not be used in either *in vitro* or *in vivo* assays for mutagenicity. This approach should be regarded as general guidance. It is important that a flexible approach is adopted, with selection of further tests being dependant upon the interpretation of results obtained at each stage.

5.4.1 *In vitro studies*

Circumstances in which required

In vitro mutagenicity tests (bacterial assay for gene mutation, test for clastogenicity in mammalian cells and test for gene mutation in mammalian cells) must always be reported.

Test Guidelines

Acceptable test guidelines are -

- EEC Method B 14 - *Salmonella Typhimurium* reverse mutation assay,
- EEC Method B 10 - *in vitro* mammalian cytogenetic test,
- Commission Directive 88/302/EEC, Part B - *in vitro* mammalian cell gene mutation test.

5.4.2 *In vivo studies in somatic cells*

Circumstances in which required

If all the results of the *in vitro* studies are negative further testing must be done, taking into consideration all other relevant information available (including toxicokinetic, toxicodynamic and physico-chemical data and data on analogous substances). The test can be an *in vivo* study or an *in vitro* study using a different metabolising system from that/those previously used.

If the *in vitro* cytogenetic test is positive, an *in vitro* test using somatic cells (metaphase analysis in rodent bone marrow or micronucleus test in rodents) must be conducted.

If either of the *in vitro* gene mutation tests is positive, an *in vivo* test to investigate unscheduled DNA synthesis or a mouse spot test must be conducted.

Test Guidelines

Acceptable test guidelines are -

- EEC Method B 12 - micronucleus test,
- Commission Directive 88/302/EEC, Part B - mouse spot test,
- EEC Method B 11 - *in vivo* mammalian bone-marrow cytogenetic test, chromosomal analysis

5.4.3 *In vivo studies in germ cells*

Circumstances in which required

When any result of an *in vivo* study in somatic cells is positive, *in vivo* testing for germ cell effects may be justified. The necessity for conducting these tests will have to be considered on a case-by-case basis, taking into account information regarding toxicokinetics, use and anticipated exposure. Suitable tests involve interaction with DNA (such as the dominant lethal assay), to assess the potential for inherited effects and possibly to make a quantitative assessment of heritable effects. It is recognized that in view of their complexity, the use of quantitative studies requires strong justification.

5.5 ***Long term toxicity and carcinogenicity***

Aim of the test

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

- identify adverse effects resulting from exposure to the active substance,
- identify target organs, where relevant,
- establish the dose-response relationship,
- identify changes in toxic signs and manifestations observed, and
- establish the NOAEL.

Similarly, the carcinogenicity studies taken together with other relevant data and information on the active substance, must be sufficient to permit the hazards for humans, following repeated exposure to the active substance, to be assessed, and in particular must be sufficient -

- to identify carcinogenic effects resulting from exposure to the active substance,
- to establish the species and organ specificity of tumours induced,
- to establish the dose-response relationship, and
- for non-genotoxic carcinogens, to identify the maximum dose eliciting no adverse effect (threshold dose).

Circumstances in which required

The long-term toxicity and carcinogenicity of all active substances must be determined. If in exceptional circumstances, it is claimed that such testing is unnecessary, that claim must be fully justified, *viz.* toxicokinetic data demonstrates that absorption of the active substance does not occur from the gut, through the skin or via the pulmonary system.

Test Conditions

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

A carcinogenicity study with the active substance, using the mouse as test species, must be conducted.

Where a non-genotoxic mechanism for carcinogenicity is suggested, a well argued case, supported with relevant experimental data, including that necessary to elucidate the possible mechanism involved, must be provided.

While the standard reference points for treatment responses are concurrent control data, historical control data may be helpful in the interpretation of particular carcinogenicity studies. Where submitted, historical control data should be from the same species and strain, maintained under similar conditions and should be from contemporaneous studies. Historical control data provided must include -

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

The doses tested, including the highest dose tested, must be selected on the basis of the results of short-term testing and where available at the time of planning the studies concerned, on the basis of metabolism and toxicokinetic data. The highest dose in the carcinogenicity study should elicit signs of minimal toxicity such as slight depression in body-weight (less than 10 %), without causing tissue necrosis or metabolic saturation and without substantially altering the normal lifespan, due to effects other than tumours. If the long-term toxicity study is carried out separately, the highest dose level should elicit definite signs of toxicity without causing excessive lethality. Higher doses, causing excessive toxicity are not considered relevant to evaluations to be made.

In the collection of data and compilation of reports, incidence of benign and malignant tumours must not be combined, unless there is clear evidence of benign tumours becoming malignant with time. Similarly, dissimilar, un-associated tumours, whether benign or malignant, occurring in the same organ must not be combined, for reporting purposes. In the interests of avoiding confusion, terminology such as that developed by the American Society of Toxicologic Pathologists [48], or the Hanover Tumour Registry (RENI) should be used in the nomenclature and reporting of tumours. The system used must be identified.

[48] Standardized System of Nomenclature and Diagnostic Criteria - Guides for Toxicologic Pathology

It is essential that biological material selected for histopathological examination includes material selected to provide further information on lesions identified during gross pathological examination. Where relevant to the elucidation of the mechanism of action and available, special histological staining) techniques, histochemical techniques and electron microscope examinations, must be conducted and reported.

Test Guideline

Commission Directive 88/302/EEC, Part B, chronic toxicity test, carcinogenicity test or combined chronic toxicity/carcinogenicity test.

5.6 ***Reproductive toxicity***

Adverse reproductive effects are of two main types -

- impairment of male or female fertility, and
- effects on the normal development of progeny (developmental toxicity).

Possible effects on all aspects of reproductive physiology in both males and females, as well as possible effects on pre-natal and post-natal development, must be investigated and reported. If in exceptional circumstances, it is claimed that such testing is unnecessary, that claim must be fully justified.

While the standard reference points for treatment responses are concurrent control data, historical control data may be helpful in the interpretation of particular reproductive studies. Where submitted, historical control data should be from the same species and strain, maintained under similar conditions and should be from contemporaneous studies. Historical control data provided must include -

- the identification of species and strain, the name of the supplier and the specific colony identification, if the supplier has more than one geographical location,
- the name of the laboratory and the dates when the study was performed,
- a description of the general conditions under which animals were maintained, including the type or brand of diet and, where possible, the amount consumed,
- the approximate age, in days, of the control animals at the beginning of the study and at the time of killing or death,
- a description of the control group mortality pattern observed during or at the end of the study, and other pertinent observations (*e.g.* diseases, infections), and
- the names of the laboratory and of the examining scientists responsible for gathering and interpreting pathological data from the study.

5.6.1 *Multi-generation studies*

Aim of the test

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

- to identify direct and indirect effects on reproduction resulting from exposure to the active substance,
- to identify any enhancement of general toxic effects (noted during short-term and chronic testing),
- to establish the dose-response relationship, to identify changes in toxic signs and manifestations observed, and
- to establish the NOAEL.

Circumstances in which required

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

Test guideline

Commission Directive 88/302/EEC, Part B, two-generation reproduction toxicity test. In addition organ weight of reproductive organs must be reported.

Supplementary studies

Where necessary for a better interpretation of effects on reproduction and as far as this information is not yet available it could be necessary to perform supplementary studies and information -

- separate male and female studies,
- three segment design studies,
- dominant lethal assay for male fertility,
- cross matings of treated males with untreated females and *vice versa*,
- effects on spermatogenesis,
- effects on oogenesis,
- sperm motility, mobility and morphology, and
- investigation of hormonal activity.

5.6.2 *Developmental toxicity studies*

Aim of the test

The studies reported, taken together with other relevant data and information on the active substance, must be sufficient to permit effects on embryonic and foetal development, following repeated exposure to the active substance, to be assessed, and in particular must be sufficient -

- to identify direct and indirect effects on embryonic and foetal development resulting from exposure to the active substance,
- to identify any maternal toxicity,
- to establish the relationship between observed responses and dose in both dam and offspring,
- to identify changes in toxic signs and manifestations observed, and
- to establish the NOAEL.

Furthermore, the tests will give additional information on any enhancement of general toxic effects in pregnant animals.

Circumstances in which required

The tests must always be carried out.

Test guideline

Commission Directive 88/302/EEC, Part B, teratogenicity test - rodent and non-rodent.

5.7 ***Delayed neurotoxicity studies***

Aim of the test

The test will provide sufficient data to establish if the active substance could provoke delayed neurotoxicity after exposure.

Circumstances in which required

These studies must be carried out for substances of similar or related structures to those known to have be capable of inducing delayed neurotoxicity, such as organophosphates.

Test Guideline

The test must be carried out in accordance with OECD Guideline 418.

5.8 ***Other toxicological studies***

5.8.1 *Toxicity studies with metabolites, as referred to in the introduction, point (vii)*

Supplementary studies, where they relate to substances other than the active substance, are not a routine requirement.

Decisions as to the need for supplementary studies must be made on a case-by-case basis.

5.8.2 *Supplementary studies on the active substance*

In certain cases it may be necessary to carry our supplementary studies to further clarify the nature of observed effects. Such studies could include -

- studies on absorption, distribution, excretion and metabolism,
- studies on neurotoxic potential,
- studies on immunotoxicological potential,
- studies using other routes of administration.

Decisions as to the need for supplementary studies must be made on a case-by-case basis, taking into account the results of the available toxicological and metabolism studies and the most important exposure routes.

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

5.9 ***Medical data***

Where available, and without prejudice to the provisions of Article 5 of Council Directive 80/1107/EEC [49], on the protection of workers from the risks related to exposure to chemical, physical and biological agents at work, practical data and information relevant to the recognition of the symptoms of poisoning, and on the effectiveness of first aid and therapeutic measures must be submitted. Specific references to the investigations relative to antidote pharmacology or safety pharmacology using animals, should be provided. Where relevant, the effectiveness of potential antagonists to poisoning should be investigated and reported.

Data and information relevant to the effects of human exposure, where available and of the necessary quality, are of particular value, in confirming the validity of extrapolations made and conclusions reached with respect to target organs, dose-response relationships, and the reversibility of toxic effects. Such data can be generated following accidental or occupational exposure.

[49] O.J. No. L327/8 3/12/1980

5.9.1 *Medical surveillance on manufacturing plant personnel*

Reports of occupational health surveillance programmes, supported with detailed information on the design of the programmes, on exposure to the active substance and exposure to other chemicals, must be submitted. Such reports should, where feasible, include data from persons exposed in manufacturing plants or after application of the active substance (*e.g.* in efficacy trials).

Available information on the sensitisation including allergenic response of workers and others exposed to the active substance, must be provided, and include where relevant details of any incidence of hypersensitivity. The information provided should include details of frequency, level and duration of exposure, the symptoms observed and other relevant clinical information.

5.9.2 *Direct observation, e.g. clinical cases and poisoning incidents*

Available reports from the open literature, relating to clinical cases and poisoning incidents, where they are from refereed journals or official reports, must be submitted, together with reports of any follow-up studies undertaken. Such reports should contain complete descriptions of the nature, level and duration of exposure, as well as the clinical symptoms observed, first aid and therapeutic measures applied and measurements and observations made. Summary and abstract information is not of value.

Where supported with the necessary level of detail, such documentation can be of particular value, in confirming the validity of extrapolations from animal data to man and in identifying unexpected adverse effects that are specific to humans.

5.9.3 *Observations on exposure of the general population and epidemiological studies if appropriate*

Where available, and supported with data on levels and duration of exposure, and where conducted in accordance with recognized standards [50], epidemiological studies are of particular value and must be submitted.

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

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

[50] Guidelines for Good Epidemiology Practices for Occupational and Environmental Research, developed by the Chemical Manufacturers Association's Epidemiology Task Force, as part of the Epidemiology Resource and Information Centre (ERIC), Pilot Project, 1991

5.9.5 *Proposed treatment: first aid measures, antidotes, medical treatment*

The first aid measures to be used in the event of poisoning (actual and suspected) and in the event of contamination of eyes must be reported.

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

5.9.6 *Expected effects of poisoning*

Where known, the expected effects and the duration of these effects following poisoning must be described and include a description of the impact of -

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

5.10 ***Summary of mammalian toxicology and overall conclusions***

A summary of all information provided in accordance with paragraphs 5.1 through 5.9 must be submitted and include a detailed and critical assessment of those data in the context of relevant evaluative and decision making criteria and guidelines, with particular reference to the risks for man and animals that may or do arise, and the extent, quality and reliability of the data base.

Where relevant, in the light of findings with respect to the analytical profile of batches of the active substance (paragraph 1.11) and any bridging studies conducted (paragraph 5 (iv)), the relevance of the data as submitted, to the toxicological profile of the active substance as manufactured, must be argued.

On the basis of an assessment of the data base, and the relevant decision making criteria and guidelines, justifications must be submitted for the NOAELs proposed for each relevant study.

On the basis of these data scientifically reasoned proposals for the estimation of the ADI and AOEL(s) for the active substance must be submitted.

6 Residues in or on treated products, food and feed

Introduction

(i) The information provided, taken together with that provided for one or more preparations containing the active substance, must be sufficient to permit an evaluation to be made as to the risks for man, arising from residues of the active substance and relevant metabolites, degradation and reaction products remaining in food. In addition, the information provided must be sufficient to:

- permit a decision to be made as to whether, or not, the active substance can be included in Annex I,
- specify appropriate conditions or restrictions to be associated with any inclusion in Annex I.

(ii) A detailed description (specification) of the material used, as provided under point I 1 must be provided.

(iii) Studies should be performed in accordance with the guidance on regulatory testing procedures for residues of plant protection products in food [51].

(iv) Where relevant, data should be analysed using appropriate statistical methods. Full details of statistical analyses carried out should be reported.

(v) Stability of residues during storage -

It may be necessary to perform studies on the stability of residues during storage. Provided samples are frozen within generally 24 hours after sampling and unless a compound is otherwise known to be volatile or labile, data are not normally required for samples extracted and analysed within 30 days from sampling (6 months in the case of radiolabelled material).

Studies with non-radiolabelled substances should be carried out with representative substrates and preferably on samples from treated crops or animals with incurred residues. Alternatively, if this is not possible, aliquots of prepared control samples should be spiked with a known amount of chemical before storage under normal storage conditions.

Where degradation during storage is significant (more than 30 %) it may be necessary to change the storage conditions or not to store the samples prior to analysis and it may be necessary to repeat studies where unsatisfactory storage conditions were used.

Detailed information with respect to sample preparation and the storage conditions (temperature and duration) of samples and extracts must be submitted. Storage stability data using sample extracts will also be required unless samples are analysed within 24 hours of extraction.

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[51] Guidelines for the generation of data concerning residues as provided in Annex II part A, section 6 and Annex III, part A, section 8 of Directive 91/414/EEC concerning the placing of plant protection products on the market [Foreword, 10 June 1999; Appendix A – Metabolism and distribution in plants, 22 July 1997;Appendix B –General recommendations for the design, preparation and realization of residue trials, 22 July 1997; Annex 2 – Classification of (minor) crops not listed in the Appendix of Council Directive 90/642; Appendix C – Testing of plant protection products in rotational crops, 22 July 1997; Appendix D – Comparability, extrapolation, group tolerances and data requirements, 12 June 2001; Appendix E – Processing studies, 22 July 1997; Appendix F – Metabolism and distribution in domestic animals, 22 July 1997; Appendix G – Livestock feeding studies, 22 July 1996; Appendix H – Storage stability of residue samples, 22 July 1997; Appendix I – Calculation of maximum residue levels and safety intervals, 22 July 1997]
http://europa.eu.int/comm/food/fs/ph_ps/pest/index_en.htm

6.1 ***Metabolism distribution and expression of residue in plants***

Aim of the tests

The objectives of these studies are:

- to provide an estimate of total terminal residues in the relevant portions of crops at harvest following treatment as proposed,
- to identify the major components of the total terminal residue,
- to indicate the distribution of residues between relevant crop parts,
- to quantify the major components of the residue and to establish the efficiency of extraction procedures for these components,
- to provide a basis for a decision as to the definition of and basis for expression of the residue.

Circumstances in which required

These studies must always be performed unless it can be justified that no residues will remain on plants/plant products that are used as food or feedingstuffs.

Test conditions

Metabolism studies have to involve crops or categories of crops in which plant protection products containing the active substance in question would be used. If a wide range of uses in different crop categories or in the category fruits is envisaged, studies have to be carried out on at least three crops unless it can be justified that different metabolic pathways are unlikely to occur. In cases where use is envisaged in different categories of crops, the studies must be conducted in crops representative of the relevant categories.

For this purpose crops can be considered as falling into one of five categories: root vegetables, leafy crops, fruits, pulses and oilseeds, cereals. If studies are available for crops from three of these categories and the results indicate that the route of degradation is similar in all three categories then it is unlikely that any more studies will be needed unless it could be expected that a different metabolic pathway will occur.

The metabolism studies must be designed such that the properties of the active substance and the intended method of application are taken into account.

An evaluation of the results obtained from the studies conducted must be submitted, having particular regard to the point and path of uptake (*e.g. via* leaves or roots), and on the distribution of residues between relevant parts of the crop at harvest (with particular emphasis on edible parts for man or animals). If the crop does not take up the active substance or relevant metabolites, this must be explained. Information on the mode of action and the physico-chemical properties of the active substance may be helpful in assessing trials data.

6.2 ***Metabolism distribution and expression of residue in livestock***

Aim of tests

The objectives of these studies are:

- to identify the major components of the total terminal residue in edible animal products,
- to quantify the rate of degradation and excretion of the total residue in certain animal products (milk or eggs) and excreta,
- to indicate the distribution of residues between relevant edible animal products,
- to quantify the major components of the residue and to show the efficiency of extraction procedures for these components,
- to generate data from which a decision on the need for livestock feeding studies as provided for in point 6.4 can be made,
- to provide a basis for a decision as to the definition of and basis for expression of the residue.

Circumstances in which required

Metabolism studies on animals, such as lactating ruminants (*e.g.* goat or cow) or laying poultry, are only required when use of plant protection products containing the active substance may lead to significant residues in livestock feed (≥ 0.1 mg/kg of the total diet as received, except special cases *e.g.* active substances which accumulate). Where it becomes apparent that metabolic pathways differ significantly in the rat as compared to ruminants, a pig study must be conducted unless the expected intake by pigs is not significant.

6.3 ***Residue trials***

Aim of the tests

The objectives of these studies are:

- to quantify the highest likely residue levels in treated crops at harvest or outloading from store, following use in accordance with the proposed good agricultural practice (GAP), and
- to determine, when appropriate, the rate of decline of residues in and/or on crops.

Circumstances in which required

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

Residue trial data must be submitted as part of the Annex 11 dossiers, for those uses of plant protection products for which authorization is sought at the same time as inclusion of the active substance in Annex I is sought.

Test conditions

Supervised trials reported should be of trials that correspond to proposed critical GAP. The test conditions must take into account the highest residues that may reasonably arise (*e.g.* maximum number of proposed applications, use of the maximum envisaged quantity, shortest pre-harvest intervals, withholding periods or storage periods) while being representative of the realistic worst-case conditions in which the active substance would be used.

Sufficient data must be generated and submitted to confirm that patterns determined hold for the regions and the range of conditions, likely to be encountered in the regions concerned for which its use is to be recommended.

When designing a supervised trial programme, factors such as climatic differences existing between production areas, differences in production methods (*e.g.* outdoor versus glasshouse uses), seasons of production, type of formulations *etc.* should normally be taken into account.

In general, for a comparable set of conditions, trials should be carried out over a minimum of two growing seasons. All exceptions should be fully justified.

The precise number of trials necessary is difficult to determine in advance of a preliminary evaluation of the trial results. Minimum data requirements only apply where comparability can be established between production areas, *e.g.* concerning climate, methods and growing seasons of production *etc.* Assuming all other variables (climate *etc.*) are comparable, a minimum of eight trials representative of the proposed growing area is required for major crops. For minor crops normally four trials representative of the proposed growing area are required.

Due to the inherently higher level of homogeneity in residues arising from post-harvest treatments or protected crops, trials from one growing season are generally acceptable.

For post-harvest treatments, in principle, a minimum of four trials are required, carried out preferably at different locations with different cultivars. A set of trials must be carried out for each application method and store type unless the worst-case residue situation can be clearly identified.

The number of studies per growing season to be performed can be reduced if it can be justified that the residue levels in plants/plant products will be lower than the limit of determination.

Where a significant part of the consumable portion of the crop is present at the time of application, half of the supervised residue trials reported should include data to show the effect of time on the level of residue present (residue decline studies) unless it can be justified that the consumable crop is not affected by the application of the plant protection product under the proposed conditions of use.

6.4 ***Livestock feeding studies***

Aim of the tests

The objective of these studies is to determine the residue in products of animal origin that will result from residues in feedingstuffs or fodder crops.

Circumstances in which required

Feeding studies are only required:

- when significant residues (≥ 0.1 mg/kg of the total diet as received, except special cases, such as active substances which accumulate) occur in crops or part of the crop (*e.g.* trimmings, waste) fed to animals, and
- when metabolism studies indicate that significant residues (0.01 mg/kg or above the limit of determination if this would be higher than 0.01 mg/kg) may occur in any edible animal tissue taking into account the residue levels in potential feedingstuffs obtained at the 1 x dose rate.

Where appropriate separate feeding studies for lactating ruminants and/or laying poultry should be submitted. Where it appears from the metabolism studies submitted in accordance with the provisions of point 6.2 that metabolic pathways differ significantly in the pig as compared to ruminants, a pig feeding study must be conducted unless the expected intake by pigs is not significant.

Test conditions

In general, the feed is administered in three dosages (expected residue level, 3-5 times, and 10 times the expected residue level). When setting the 1 x dose, a theoretical feed ration must be compiled.

6.5 ***Effects of industrial processing and/or household preparations***

Circumstances in which required

The decision as to whether it is necessary to carry out processing studies will depend on:

- the importance of a processed product in the human or animal diet,
- the level of residue in the plant or plant product to be processed,
- the physico-chemical properties of the active substance or relevant metabolites, and
- the possibility that degradation products of toxicological significance may be found after processing of the plant or plant product.

Processing studies are not normally necessary if no significant or no analytically determinable residues occur in the plant or plant product which would be processed, or if the total theoretical maximum daily intake (TMDI) is less than 10 % of the ADI. In addition processing studies are not normally required for plants or plant products which are mostly eaten raw except for

those with inedible portions such as citrus, banana or kiwi fruit where data on the distribution of the residue in peel/pulp may be required.

'Significant residues' generally refer to residues above 0.1 mg/kg. If the pesticide concerned has a high acute toxicity and/or a low ADI, consideration must be given to conducting processing studies for determinable residues below 0.1 mg/kg.

Studies of the effects on the nature of the residue are not normally required where only simple physical operations, not involving a change in temperature of the plant or the plant product, are involved, such as washing, trimming or pressing.

6.5.1 *Effects on the nature of the residue*

Aim of the tests

The objective of these studies is to establish whether or not breakdown or reaction products arise from residues in the raw products during processing that may require a separate risk assessment.

Test conditions

Depending upon the level and chemical nature of the residue in the raw commodity, a set of representative hydrolysis situations (simulating the relevant processing operations) should be investigated, where appropriate. The effects of processes other than hydrolysis, may also have to be investigated, where the properties of the active substance or metabolites indicate that toxicologically significant degradation products may occur as a result of these processes. The studies are normally conducted with a radiolabelled form of the active substance.

6.5.2 *Effects on the residue levels*

Aim of the tests

The main objectives of these studies are:

- to determine the quantitative distribution of residues in the various intermediate and end products, and to estimate relevant transfer factors, and
- to enable a more realistic estimate to be made of the dietary intake of residues.

Test conditions

Processing studies should represent household processing and/or actual industrial processes.

In the first instance it is usually only necessary to carry out a core set of "balance studies" representative of the common processes relevant to plants or plant products that contain significant residues. A justification must be provided for the selection made. The technology to be used in processing studies should always correspond as closely as possible to the actual conditions that are normally used in practice. A balance sheet should be made in which the mass balance of residues in all intermediate and end products is investigated. In drawing up such a balance sheet any concentrations or reductions in residues in individual products can be recognised and the corresponding transfer factors can also be determined.

If the processed plant products play an important part in the diet, and if the "balance study" indicates that a significant transfer of residue into the processed products could occur, then three "follow-up studies" to determine residue concentration or dilution factors must be carried out.

6.6 ***Residues in succeeding crops***

Aim of the test

The objective of these studies is to permit an evaluation to be made as to the residue levels likely to occur in succeeding crops.

Circumstances in which required

Where data generated in accordance with Annex IIA point 7.1 or Annex IIIA point 9.1, shows that significant residues (> 10 % of the applied active substance - total of unchanged active substance and relevant metabolites or degradation products) remain in soil or in plant materials, such as straw or organic material up to sowing or planting time of possible succeeding crops, and which could lead to residues above the limit of determination in succeeding crops at harvest, consideration must be given to the residue situation. This should include consideration of the nature of the residue in the succeeding crops and involve at least a theoretical estimation of the level of these residues. If the likelihood of residues in succeeding crops cannot be excluded, metabolism and distribution studies should be carried out, if necessary followed by field trials.

Test conditions

If a theoretical estimation of residues in succeeding crops is carried out, full details of the estimations and a justification for the conclusions reached, must be provided.

Metabolism and distribution studies and field trials, if necessary, must be carried out on representative crops chosen to represent normal agricultural practice.

6.7 ***Proposed maximum residue levels (MRLs) and residue definition***

A full justification for the proposed MRLs must be provided, including, where relevant, full details of the statistical analysis used.

When judging which compounds are to be included in the residue definition, account must be taken of the toxicological significance of the candidate compounds, the amounts likely to be present and the practicality of the analytical methods proposed for post-registration control and monitoring purposes.

6.8 ***Proposed pre-harvest intervals for envisaged uses, or withholding periods or storage periods, in the case of post-harvest uses***

A full justification for the proposals must be provided.

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

Consideration must be given to the calculation of realistic dietary intake levels. This may be done in a step-wise fashion leading to increasingly realistic predictions of intake. Where relevant, other sources of exposure such as residues arising from the use of medicines or veterinary drugs must be taken into account.

6.10 ***Summary and evaluation of residue behaviour***

A summary and evaluation of all data presented under point 6 must be provided. It must be carried out and be presented in accordance with the guidance provided by the competent authority. It should include a detailed and critical assessment of the data in the context of relevant evaluative and decision making criteria and guidelines, having particular regard to the risks for man and animals that may or do arise, and the extent, quality and reliability of the data base.

In particular the toxicological significance of any non-mammalian metabolites must be addressed.

A schematic diagram should be prepared of the metabolic pathway in plants and animals with a brief explanation of the distribution and chemical changes involved.

7 **Fate and behaviour in the environment**

Introduction

(i) The information provided, taken together with that for one or more preparations containing the active substance, must be sufficient to permit an assessment of the fate and behaviour of the active substance in the environment, and of the non-target species likely to be at risk from exposure to the active substance, its metabolites, degradation and reaction products, where they are of toxicological or environmental significance.

(ii) In particular, the information provided for the active substance, together with other relevant information and that provided for one or more preparations containing it, must be sufficient -

- to decide whether, or not, the active substance can be included in Annex 1,
- to specify appropriate conditions or restrictions to be associated with any inclusion in Annex 1,
- to classify the active substance as to hazard;
- to specify the hazard symbols, the indications of danger, and relevant risk and safety phrases for the protection of the environment, which are to be included on packaging (containers),
- to predict the distribution, fate, and behaviour in the environment of the active substance and relevant metabolites, degradation and reaction products as well as the time courses involved,
- to identify non-target species and populations for which hazards arise because of potential exposure, and
- to identify measures necessary to minimize contamination of the environment and impact on non-target species.

(iii) A detailed description (specification) of the material used, as provided for under Section 1, point 11 must be provided. Where testing is done using active substance the material used should be of that specification that will be used in the manufacture of preparations to be authorized except where radiolabelled material is used.

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

(iv) Where radiolabelled test material is used, radiolabels should be positioned at sites (one or more as necessary), to facilitate elucidation of metabolic and degradative pathways and to facilitate investigation of the distribution of the active substance and of its metabolite, reaction and degradation products in the environment.

(v) It may be necessary to conduct separate studies for metabolites, degradation or reaction products, where these products can constitute a relevant risk to non-target organisms or to the quality of water, soil and air and where their effects cannot be evaluated by the available results relating to the active substance. Before such studies are performed the information from Sections 5 and 6 must be taken into account.

(vi) Where relevant, tests must be designed and data analysed using appropriate statistical methods. Full details of the statistical analysis carried out must be reported (*e.g.* all point estimates must

be given with confidence intervals, exact p-values must be given rather than stating significant/non significant).

7.1 ***Fate and behaviour in soil***

All relevant information on the type and the properties of the soil used in the studies, including pH, organic carbon content, cation exchange capacity, particle size distribution and water holding capacity. Particle size distribution and water holding capacity at pF = 0 and pF = 2.5 must be reported in accordance with relevant ISO or other international standards.

The microbial biomass of soils used for laboratory degradation studies must be determined just prior to the commencement and at the end of the study.

It is recommended that the same soils be used throughout all laboratory soil studies.

The soils used for degradation or mobility studies must be selected such that they are representative of the range of soils typical of the various Community regions where use exists or is anticipated, and be such that:

- they cover a range of organic carbon content, particle size distribution and pH values; and
- where an the basis of other information, degradation or mobility are expected to be pH dependent (*e.g.* solubility and hydrolysis rate - paragraphs 2.7 and 2.8), they cover the following pH ranges -

  4.5 to 5.5,

  6 to 7, and

  8 (approximately).

Soils used must, wherever possible, be freshly sampled. If use of stored soils is unavoidable, storage should be properly carried out for a limited time under defined and reported conditions. Soils stored for longer periods of time can only be used for adsorption/desorption studies.

The soil chosen to commence the programme of studies required should not have extreme characteristics with respect to parameters such as particle size distribution, organic carbon content and pH.

Soils should be collected and handled in accordance with ISO 10381-6 (*Soil quality - Sampling - Guidance on the collection, handling and storage of soil for the assessment of microbial processes in the laboratory*). Any deviations must be reported and justified.

Field studies should be carried out in conditions as close to normal agricultural practice as possible on a range of soil types and climatic conditions representative of the area(s) of use. Weather conditions shall be reported in cases where field studies are conducted.

7.1.1 *Route and rate of degradation*

7.1.1.1 *Route of degradation*

Aim of the tests

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

- identify, where feasible, the relative importance of the types of process involved (balance between chemical and biological degradation),
- identify the individual components present which at any time account for more than 10% of the amount of active substance added, including, where feasible, non-extractable residues,
- identify where possible also individual components present which account for less than 10% of the amount of active substance added,
- establish the relative proportions of the components present (mass balance), and
- permit the soil residue of concern and to which non-target species are or may be exposed, to be defined.

Where a reference is made to non-extractable residues these are defined as chemical species originating from pesticides used according to 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 generated through metabolic pathways leading to natural products.

7.1.1.1.1 *Aerobic degradation*

Circumstances in which required

The degradation pathway or pathways must always be reported except where the nature and manner of use of preparations containing the active substance, preclude soil contamination such as uses on stared products or wound healing treatments for trees.

Test conditions

The degradation pathway or pathways must be reported for one soil.

Results obtained must be presented in the form of schematic drawings showing the pathways involved, and in the form of balance sheets that show the distribution of radiolabel as a function of time, as between:

- active substance,
- $C0_2$,
- volatile compounds other than $C0_2$,
- individual identified transformation products,
- extractable substances not identified, and
- non-extractable residues in soil.

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

The duration of the study is normally 120 days, except where after a shorter period the levels of non-extractable residues and CO_2, are such that they can be extrapolated in a reliable way to 100 days.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides[52].

7.1.1.1.2 *Supplementary studies*

Anaerobic degradation

Circumstances in which required

An anaerobic degradation study must be reported unless it can be justified that exposure of plant protection products containing the active substance to anaerobic conditions is unlikely to occur.

Test conditions and test guideline

The same provisions as provided for under the corresponding paragraph of point 7.1.1.1.1 apply.

Soil photolysis

Circumstances in which required

A soil photolysis study must be reported unless it can be justified that deposition of the active substance at the soil surface is unlikely to occur.

[52] Society of Environmental Toxicology and Chemistry (SETAC), 1995. Procedures for assessing the environmental fate and ecotoxicity of pesticides, ISBN 90-5607-002-9

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

7.1.1.2 *Rate of degradation*

7.1.1.2.1 *Laboratory studies*

Aim of the tests

The soil degradation studies should provide the best possible estimates of the time taken for degradation of 50% and 90% (DT_{50lab} and DT_{90lab}), of the active substance, and of relevant metabolites, degradation and reaction products under laboratory conditions.

Aerobic degradation

Circumstances in which required

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

Test conditions

The rate of aerobic degradation of the active substance in three soil types additional to that referred to in paragraph 7.1.1.1.1 must be reported.

In order to investigate the influence of temperature on degradation, one additional study at 10 °C must be performed on one of the soils used for the investigation of degradation at 20 °C unless a validated Community calculation model for the extrapolation of degradation rates to low temperatures is available.

The duration of the study is normally 120 days except where more than 90% of the active substance is degraded before that period expires.

Similar studies for three soil types must be reported for all relevant metabolites, degradation and reaction products which occur in soil and which at any time during the studies account for more than 10% of the amount of active substance added, except where their DT_{50} values were determined from the results of the degradation studies with the active substance.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

Anaerobic degradation

Circumstances in which required

The rate of anaerobic degradation of the active substance must be reported where an anaerobic study has to be performed according to point 7.1.1.1.2.

Test conditions

The rate of anaerobic degradation of the active substance must be determined in the soil used in the anaerobic study performed according to point 7.1.1.1.2.

The duration of the study is normally 120 days except where more than 90% of the active substance is degraded before that period expires.

Similar studies for one soil must be reported for all relevant metabolites, degradation and reaction products which occur in soil and which at any time during the studies account for more than 10% of the amount of active substance added, except where their DT_{50} values were determined from the results of the degradation studies with the active substance.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

7.1.1.2.2 *Field studies*

Soil dissipation studies

Aim of the test

The soil dissipation studies should provide estimates of the time taken for dissipation of 50% and 90% (DT_{50f} and DT_{90f}), of the active substance under field conditions. Where relevant, information on relevant metabolites, degradation and reaction products must be reported.

Circumstances in which required

The tests have to be conducted in those conditions where the DT_{50lab} determined at 20 °C and at a moisture content of the soil related to a pF value of 2 - 2.5 (suction pressure) is greater than 60 days.

Where plant protection products containing the active substance are intended to be used in cold climatic conditions, the tests have to be conducted where the DT_{50lab} determined at 10 °C and at a moisture content of the soil related to a pF value of 2 - 2.5 (suction pressure) is greater than 90 days.

Test conditions

Individual studies on a range of representative soils (normally four different types) must be continued until > 90% of the amount applied has dissipated. The maximum duration of the studies is 24 months.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

Soil residue studies

Aim of the test

Soil residue studies should provide estimates of the soil residue levels at harvest or at time of sowing or planting succeeding crops.

Circumstances in which required

Soil residue studies must be reported where the DT_{50lab} is greater than one-third of the period between application and harvest and where absorption by the succeeding crop is possible, except where soil residues at sowing or planting of a succeeding crop can be reliably estimated from the data of the soil dissipation studies or where it can be justified that these residues can not be phytotoxic to or leave unacceptable residues in rotational crops.

Test conditions

Individual studies must be continued until harvest or time of sowing or planting succeeding crops, unless > 90 % of the amount applied has dissipated.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

Soil accumulation studies

Aim of the tests

The tests should provide sufficient data to evaluate the possibility of accumulation of residues of the active substance and of relevant metabolites, degradation and reaction products.

Circumstances in which required

Where on the basis of soil dissipation studies it is established that DT_{90f} > one year and where repeated application is envisaged, whether in the same growing season or in succeeding years, the possibility of accumulation of residues in soil and the level at which a plateau concentration is achieved must be investigated except where reliable information can be provided by a model calculation or another appropriate assessment.

Test conditions

Long-term field studies must be carried out on two relevant soils and involve multiple applications.

Before performing these studies the applicant shall seek the agreement of the competent authorities on the type of study to be performed.

7.1.2 *Adsorption and desorption*

Aim of the test

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

Circumstances in which required

The studies must always be reported except where the nature and manner of use of preparations containing the active substance preclude soil contamination such as uses on stared products or wound healing treatments for trees.

Test conditions

Studies on the active substance must be reported for four soil types.

Similar studies, for at least three soil types, must be reported for all relevant metabolites, degradation and reaction products which in soil degradation studies, account at any time for more than 10% of the amount of active substance added.

Test guideline

OECD method 106.

7.1.3 *Mobility in the soil*

7.1.3.1 *Column leaching studies*

Aim of the test

The test should provide sufficient data to evaluate the mobility and leaching potential of the active substance and if possible of relevant metabolites, degradation and reaction products.

Circumstances in which required

Studies in four soils must be carried out where in the absorption and desorption studies provided for under point 7.1.2 it is not possible to obtain reliable absorption coefficient values.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

7.1.3.2 *Aged residue column leaching*

Aim of the test

The test should provide sufficient data to estimate the mobility and leaching potential of relevant metabolites, degradation and reaction products.

Circumstances in which required

The studies must be performed except:

- where the nature and manner of use of preparations containing the active substance, preclude soil contamination such as uses on stored products or wound healing treatments for trees, or
- where a separate study for the metabolite, degradation or reaction product in accordance with point 7.1.2 or 7.1.3.1 was performed.

Test conditions

The period(s) of ageing should be determined from inspection of the degradation patterns of active substance and metabolites to ensure that a relevant spectrum of metabolites is present at the time of leaching.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

7.1.3.3 *Lysimeter studies or field leaching studies*

Aim of the tests

The test should provide data on -

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

Circumstances in which required

Expert judgement will be necessary to decide whether lysimeter studies or field leaching studies should be carried out, taking into account the results of degradation and other mobility studies and the predicted environmental concentrations in ground water (PEC_{GW}) calculated in accordance with the provisions of Annex III, Section 9. The type and conditions of the study to be conducted should be discussed with the competent authorities.

Test conditions

Great care is necessary in the design of both experimental installations and individual studies, to ensure that results obtained can be used for assessment purposes. Studies should cover the realistic worst-case situation likely to arise, taking into account the soil type, climatic conditions, application rate and frequency and period of application.

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

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

Lysimeter studies

Test conditions

The minimal depth of the lysimeters should be 100 cm; their maximal depth should be 130 cm. The soil column must be undisturbed. Soil temperatures must be similar to those pertaining in the field. Where necessary, supplementary irrigation must be provided to ensure optimal plant growth and to ensure that the quantity of infiltration water is similar to that in the regions for which authorization is sought. When during the study the soil has to be disturbed for agricultural reasons it must not be disturbed to a dept deeper than 25 cm.

Field leaching studies

Test conditions

Information on the ground water table in the experimental fields must be submitted. If soil cracking is observed during the study this must be fully described.

Great attention should be given to the number and the location of water collection devices. The placement of these devices in the soil must not result in preferential flow paths.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

7.2 ***Fate and behaviour in water and air***

Aim of the tests

The information and data provided, taken together with that provided for one or more preparations containing the active substance, and other relevant information, should be sufficient to establish, or permit estimation of:

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

7.2.1 *Route and rate of degradation in aquatic systems (as far as not covered by point 2.9)*

Aim of the tests

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

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

7.2.1.1 *Hydrolytic degradation*

Circumstances in which required

The test must always be performed for relevant metabolites, degradation and reaction products which account at any time for more than 10% of the amount of active substance added unless sufficient information on their degradation is available from the test performed in accordance with point 2.9.1.

Test conditions and test guideline

The same provisions as provided under the corresponding paragraphs of point 2.9.1 apply.

7.2.1.2 *Photochemical degradation*

Circumstances in which required

The test must always be performed for relevant metabolites, degradation and reaction products which account at any time for more than 10% of the amount of active substance added unless sufficient information an their degradation is available from the tests performed in accordance with points 2.9.2 and 2.9.3.

Test conditions and test guideline

The same provisions as provided under the corresponding paragraphs of points 2.9.2 and 2.9.3 apply.

7.2.1.3 *Biological degradation*

7.2.1.3.1 *"Ready biodegradability"*

Circumstances in which required

The test must always be performed unless it is not required under the provisions of Annex VI to the Directive of 1967 for the classification of the active substance.

Test guideline

EEC method C4.

7.2.1.3.2 *Water/sediment study*

Circumstances in which required

The test must be reported unless it can be justified that contamination of surface water will not occur.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

7.2.1.4 *Degradation in the saturated zone*

Circumstances in which required

Transformation rates in the saturated zone of active substances and of relevant metabolites, degradation and reaction products can provide useful information on the fate of these substances in the ground water.

Test conditions

Expert judgement is required to decide whether this information is necessary. Before performing these studies the applicant shall seek the agreement of the competent authorities on the type of study to be performed.

7.2.2 *Route and rate of degradation in air (as far as not covered by point 2.10)*

Guidance under development.

7.3 ***Definition of the residue***

In the light of the chemical composition of residues that occur in soil, water or air, resulting from use, or proposed use, of plant protection products containing the active substance a proposal for the definition of the residue must be submitted, taking account of both the levels found and their toxicological and environmental significance.

7.4 ***Monitoring data***

Available monitoring data concerning fate and behaviour of the active substance and relevant metabolites, degradation and reaction products must be reported.

8 Ecotoxicological studies

Introduction

(i) The information provided, taken together with that for one or more preparations containing the active substance, must be sufficient to permit an assessment of the impact on non-target species (flora and fauna), likely to be at risk from exposure to the active substance, its metabolites, degradation and reaction products, where they are of environmental significance. Impact can result from single, prolonged or repeated exposure and can be reversible or irreversible.

(ii) In particular, the information provided for the active substance, together with other relevant information, and that provided for one or more preparations containing it, should be sufficient to:

- decide whether, or not, the active substance can be included in Annex I,
- specify appropriate conditions or restrictions to be associated with any inclusion in Annex I,
- permit an evaluation of short- and long-term risks for non-target species - populations, communities, and processes - as appropriate,
- classify the active substance as to hazard,
- specify the precautions necessary for the protection of non-target species, and
- specify the hazard symbols, the indications of danger, and relevant risk and safety phrases for the protection of the environment, to be mentioned on packaging (containers).

(iii) There is a need to report all potentially adverse effects found during routine ecotoxicological investigations and to undertake and report, where required by the competent authority, such additional studies that may be necessary to investigate the probable mechanisms involved and to assess the significance of these effects. All available biological data and information that are relevant to the assessment of the ecotoxicological profile of the active substance must be reported.

(iv) The information on fate and behaviour in the environment, generated and submitted in accordance with points 7.1 to 7.4, and on residue levels in plants generated and submitted in accordance with point 6 is central to the assessment of impact on non-target species, in that together with information on the nature of the preparation and its manner of use, it defines the nature and extent of potential exposure. The toxicokinetic and toxicological studies and information submitted in accordance with points 5.1 to 5.8 provide essential information as to toxicity to vertebrate species and the mechanisms involved.

(v) Where relevant, tests should be designed and data should be analysed using appropriate statistical methods. Full details of the statistical analysis should be reported (*e.g.* all point estimates should be given with confidence intervals, exact p-values should be given rather than stating significant/non significant).

Test substance

(vi) A detailed description (specification) of the material used, as provided for under point 1.11 must be provided. Where testing is done using active substance the material used should be of that specification that will be used in the manufacture of preparations to be authorised except where radiolabelled material is used.

(vii) Where studies are conducted using active substance produced in the laboratory or in a pilot plant production system, the studies must be repeated using active substance as manufactured, unless it can be justified that the test material used is essentially the same, for the purposes of ecotoxicological testing and assessment. In cases of uncertainty, appropriate bridging studies must be submitted to serve as a basis for a decision as to the possible need for repetition of the studies.

(viii) In the case of studies in which dosing extends over a period, dosing should preferably be done using a single batch of active substance if stability permits.

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

(ix) For all feeding studies, average achieved dose must be reported, including where possible the dose in mg/kg body weight. Where dosing *via* the diet is utilized the test compound must be distributed uniformly in the diet.

(x) It may be necessary to conduct separate studies for metabolites, degradation or reaction products, where these products can constitute a relevant risk to non-target organisms and where their effects cannot be evaluated on the basis of available results relating to the active substance. In assessing the need for such studies, consideration must be given to the information provided in accordance with the provisions of Sections 5, 6 and 7 must be taken into account.

Test organisms

(xi) In order to facilitate the assessment of the significance of tests results obtained, including the estimation of intrinsic toxicity and the factors affecting toxicity, the same strain (or recorded origin) of each relevant species should, where possible, be used in the various toxicity tests specified.

8.1 *Effects an birds*

8.1.1 *Acute oral toxicity*

Aim of the test

The test should provide, where possible, LD_{50} values, the lethal threshold dose, time courses of response and recovery and the NOEL, and must include relevant gross pathological findings.

Circumstances in which required

The possible effects of the active substance on birds must be investigated except where the active substance is intended solely to be included in preparations for exclusive use in enclosed spaces (*e.g.* in glasshouses or in food storage practice).

Test conditions

The acute oral toxicity of active substance to a quail species - Japanese quail (*Coturnix coturnix japonica)* or Bobwhite quail (*Colinus virginianus*) - or to mallard duck (*Anas platyrhynchos*) must be determined. The highest dose used in tests need not exceed 2,000 mg/kg body weight.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

8.1.2 *Short-term dietary toxicity*

Aim of the test

The test should provide the short-term dietary toxicity (LC_{50} values, lowest lethal concentration (LLC), where possible no observed effect concentrations (NOEC), time courses of response and recovery) and include relevant gross pathological findings.

Circumstances in which required

The dietary (five-day) toxicity of the active substance to birds must always be investigated on one species except where a study in accordance with the provisions of point 8.1.3 is reported. Where its acute oral NOEL is ≤ 500 mg/kg body weight or where the short-term NOEC < 500 mg/kg food the test must be performed on a second species.

Test conditions

The first species to be studied must be either a quail species or mallard duck. If a second species must be tested it should not be related to the first species tested.

Test guideline

The test must be carried out in accordance with OECD Method 205.

8.1.3 *Sub chronic toxicity and reproduction*

Aim of the test

The test should provide a basis for assessment of the sub chronic toxicity and reproductive toxicity of the active substance to birds.

Circumstances in which required

The sub chronic and reproductive toxicity of the active substance to birds must be investigated, unless it can be justified that continued or repeated exposure of adults, or exposure of nest sites during the breading season is unlikely to occur.

Test guideline

The test must be carried out in accordance with OECD Method 206.

8.2 ***Effects on aquatic organisms***

The data of the tests referred to in points 8.2.1, 8.2.4 and 8.2.6 must be submitted for every active substance even when it is not expected that plant protection products containing it could reach surface water following the proposed conditions of use. These data are required under the provisions of Annex VI to Directive of 1967 for the classification of the active substance.

Data reported must be supported with analytical data on concentrations of the test substance in the test media.

8.2.1 *Acute toxicity to fish*

Aim of the test

The test should provide a basis for assessment of acute toxicity (LC_{50}), and include details of observed effects.

Circumstances in which required

The test must always be carried out.

Test conditions

The acute toxicity of the active substance must be determined for rainbow trout (*Oncorhynchus mykiss*) and for a warm water fish species. Where tests with metabolites, degradation or reaction products have to be performed the species used must be the more sensitive of the two species tested with the active substance.

Test guideline

The test must be carried out in accordance with EEC Method C 1.

8.2.2 *Chronic toxicity to fish*

Circumstances in which required

A chronic toxicity study must be carried out unless it can be justified that continued or repeated exposure of fish is unlikely to occur or unless a suitable microcosm or mesocosm study is available.

Expert judgment is required to decide which test has to be performed. In particular for active substance for which there are indications of particular concerns (related to the toxicity of the active substance for fish or the potential exposure) the applicant shall seek the agreement of the competent authority on the type of test to be performed.

A fish early life stage toxicity test might be appropriate where bioconcentration factors (BCF) are between 100 and 1,000 or where the EC_{50} of the active substance < 0.1 mg/L.

A fish life cycle test might be appropriate in cases where

- the bioconcentration factor is greater than 1,000 and the elimination of the active substance during a deputation phase of 14 days is lower than 95%, or
- the substance is stable in water or sediment (DT_{90} > 100 days).

It is not necessary to perform a chronic toxicity test on juvenile fish when a fish early life stage toxicity test or a fish life cycle test has been performed; it is likewise not necessary to perform a fish early life stage toxicity test when a fish life cycle test has been performed.

8 2.2. 1 *Chronic toxicity test on juvenile fish*

Aim of the test

The test should provide a basis for assessment of effects on growth, the threshold level for lethal effects and for observed effects, the NOEC and details of observed effects.

Test conditions

The test must be conducted on juvenile rainbow trout, following exposure of 28 days to the active substance. Data on the effects on growth and behaviour must be generated.

8.2.2.2 *Fish early life stage toxicity test*

Aim of the test

The test should provide a basis for assessment of effects on development, growth and behaviour, the NOEC and details of observed effects on fish early life stages.

Test guideline

The test must be carried out in accordance with OECD Method 210.

8.2.2.3 *Fish life cycle test*

Aim of the test

The test should provide a basis for assessment of effects on reproduction of the parental and on the viability of the filial generation.

Test conditions

Before performing these studies the applicant shall seek the agreement of the competent authority on the type and conditions of the study to be performed.

8.2.3 *Bioconcentration in fish*

Aim of the test

The test should permit estimation of the steady-state bioconcentration factors, uptake rate constants and deputation rate constants, for each test compound, as well as relevant confidence limits.

Circumstances in which required

The bioconcentration potential of active substances, of metabolites and of degradation and reaction products, likely to partition into fatty tissues (such as log $P_{OW} \geq 3$ - see point 2.8 or other relevant indications of bioconcentration), must be investigated and be reported, unless it can be justified that exposure leading to bioconcentration is not likely to occur.

Test guideline

The test must be carried out in accordance with OECD Method 305E.

8.2.4 *Acute toxicity to aquatic invertebrates*

Aim of the test

The test should provide an indication of the 24 and 48 hour acute toxicity of the active substance, expressed as the m6dian effective concentration (EC_{50}) for immobilization, and where possible the highest concentration causing no immobilization.

Circumstances in which required

The acute toxicity must always be determined for *Daphnia* (preferably *Daphnia magna*). Where plant protection products containing the active substance are intended to be used directly on surface water additional data must be reported on at least one representative species from each of the following groups: aquatic insects, aquatic crustaceans (on a species not related to *Daphnia*) and aquatic gastropod molluscs.

Test guideline

The test must be carried out in accordance with EEC Method C 2.

8.2.5 *Chronic toxicity to aquatic invertebrates*

Aim of the test

The test should provide where possible EC_{50} values for effects such as immobilization and reproduction and the highest concentration at which no effect such as on mortality or reproduction occurs (NOEC) and details of observed effects.

Circumstances in which required

A test on *Daphnia* and on at least one representative aquatic insect species and an aquatic gastropod mollusc species must be carried out unless it can be justified that continued or repeated exposure is not likely to occur.

Test conditions

The test with Daphnia must be continued for 21 days.

Test guideline

The test must be carried out in accordance with OECD Method 202, Part II.

8.2.6 *Effects on algal growth*

Aim of the test

The test should provide EC_{50} values for growth and growth rate, NOEC values, and details of observed effects.

Circumstances in which required

Possible effects on algal growth of active substances must always be reported. For herbicides a test on a second species from a different taxonomic group must be performed.

Test guideline

The test must be carried out in accordance with EEC Method C 3.

8.2.7 *Effects on sediment dwelling organisms*

Aim of test

The test should provide a measure of effects on survival and development (including effects on emergence of adults for *Chironomus*), the relevant EC_{50} values and NOEC values.

Circumstances in which required

Where environmental fate and behaviour data required in accordance with point 7 supports the conclusion that an active substance is likely to partition to and persist in aquatic sediments, expert judgment should be used to decide whether an acute or a chronic sediment toxicity test is required. Such expert judgment should take into account whether effects on sediment dwelling invertebrates are likely by comparing the aquatic invertebrate toxicity EC_{50} data from points 8.2.4 and 8.2.5 with the predicted levels of the active substance in sediment from data in Annex III, point 9.

Test conditions

Before performing these studies the applicant must seek the agreement of the competent authority on the type and conditions of the study to be performed.

8.2.8 *Aquatic plants*

A test on aquatic plants has to be performed for herbicides.

Before performing these studies the applicant must seek the agreement of the competent authority on the type and conditions of the study to be performed.

8.3 ***Effect on arthropods***

8.3.1 *Bees*

8.3.1.1 *Acute toxicity*

Aim of the test

The test should provide a basis for estimation of the acute oral and contact LD_{50} values of the active substance.

Circumstances in which required

Potential impact on bees must be investigated, except where preparations containing the active substance are for exclusive use in situations where bees are not likely to be exposed such as:

- food storage in enclosed spaces,
- non-systemic seed dressings,
- non-systemic preparations for application to soil,
- non-systemic dipping treatments for transplanted crops and bulbs,
- wound sealing and healing treatments,
- rodenticidal baits,
- use in glasshouses without pollinators.

Test guideline

The test must be carried out in accordance with EPPO Guideline 170.

8.3.1.2 *Bee brood feeding test*

Aim of the test

The test should provide sufficient information to evaluate possible risks from the plant protection product on honeybee larvae.

Circumstances in which required

The test must be carried out when the active substance may act as an insect growth regulator unless it can be justified that it is not likely that bee brood would be exposed to it.

Test guideline

The test must be carried out in accordance with the ICPBR Method (P.A. Oornen, A. de Riujter and J. van der Steen. Method for honeybee brood feeding tests with insect growth-regulating insecticides. *EPPO Bulletin*, Volume 22, pp.613 to 616, 1992).

8.3.2 *Other arthropods*

Aim of the test

The test should provide sufficient information to evaluate the toxicity (mortality and sub lethal effects) of the active substance to selected arthropod species.

Circumstances in which required

Effects on non-target terrestrial arthropods (*e.g.* predators or parasitoids of harmful organisms) must be investigated. The information obtained for these species can also be used to indicate the potential for toxicity to other non-target species inhabiting the same environment. This information is required for all active substances except where preparations containing the active substance are for exclusive use in situations where non-target arthropods are not exposed such as:

- food storage in enclosed spaces,
- wound sealing and healing treatments,
- rodenticidal baits.

Test conditions

Testing must initially be performed initially in the laboratory on an artificial substrate (*i.e.* glass plate or quartz sand, as appropriate) unless adverse effects can be clearly predicted from other studies. In these cases, more realistic substrates may be used.

Two sensitive standard species, a parasitoid and predatory mite (*e.g. Aphidius rhopalosiphi* and *Typhlodromus pyri*) should be tested. In addition to these, two additional species must also be tested, which should be relevant to the intended use of the substance. Where possible and if appropriate, they should represent the other two major functional groups, ground dwelling predators and foliage dwelling predators. Where effects are observed with species relevant to the proposed use of products containing the active substance, further testing may be carried out at the extended laboratory/semi-field level. Selection of the relevant test species should follow the proposals outlined in the SETAC - Guidance document on regulatory testing procedures for pesticides with non-target arthropods [53]. Testing must be conducted at rates equivalent to the highest rate of field application to be recommended.

[53] From the workshop European Standard Characteristics of beneficials Regulatory Testing (Escort), 29 to 30 March 1994, ISBN 0-95-22535-2-6.

Test guideline

Where relevant, testing should be done according to appropriate guidelines that satisfy at least the requirements for testing as included in the SETAC - Guidance document on regulatory testing procedures for pesticides with non-target arthropods.

8.4 ***Effects an earthworms***

8.4.1 *Acute toxicity*

Aim of the test

The test should provide a basis for estimation of the LC_{50} value of the active substance to earthworms, where possible the highest concentration causing no mortality and the lowest concentration causing 100% mortality, and must include observed morphological and behavioural effects.

Circumstances in which required

Effects on earthworms must be investigated, where preparations containing the active substance are applied to soil, or can contaminate soil.

Test guideline

The test must be carried out in accordance with Commission Directive 88/302/EEC, Part C, Toxicity for earthworms: Artificial soil test.

8.4.2 *Sub lethal effects*

Aim of the test

The test should provide the an estimate of the NOEC and a basis for assessment of effects on growth, reproduction and behaviour.

Circumstances in which required

Where on the basis of the proposed manner of use of preparations containing the active substance or an the basis of its fate and behaviour in soil (DT_{90}) > 100 days), continued or repeated exposure of earthworms to the active substance, or to significant quantities of metabolites, degradation or reaction products, can be anticipated expert judgment is required to decide whether a sub lethal test can be useful.

Test conditions

The test must be carried out on *Eisenia foetida*.

8.5 ***Effects on soil non-target micro-organisms***

Aim of the test

The test should provide sufficient data to permit evaluation of the impact of the active substance on soil microbial activity, in terms of nitrogen transformation and carbon mineralization.

Circumstances in which required

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

Test conditions

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

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

8.6 ***Effects on other non-target organisms (flora and fauna) believed to be at risk***

A summary of available data from preliminary tests used to assess the biological activity and dose range finding, whether positive or negative, which may provide information with respect to possible impact on other non-target species, both flora and fauna, must be provided, together with a critical assessment as to its relevance to potential impact on non-target species.

8.7 ***Effects on biological methods for sewage treatment***

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

9 **Summary and evaluation of points 7 and 8**

10 **Proposals including justification for the proposals for the classification and labelling of the active substance in accordance with the Directive of 1967 -**

- Hazard symbol(s)
- Indications of danger
- Risk phrases
- Safety phrases

11 **A dossier as referred to in Annex III, Part A, for a representative plant protection product**

PART B

Micro-organisms

Introduction

(i) Active substances can be chemical substances or micro-organisms including viruses. The data and information required for active substances consisting of micro-organisms, including viruses are set out hereunder.

For the purposes of Part B, of this Annex, the term micro-organism is defined as:

"*a microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material*"

The definition applies to, but is not limited to, bacteria, fungi, protozoa, viruses and viroids.

(ii) For all micro-organisms that are the subject of an application, all available relevant knowledge and information in the open literature should be provided.

The most important and informative information to be provided is that relating to the characterization and identification of the micro-organism. That information is described in Sections 1 to 3 (identity, biological properties and further information) and forms the basis for an assessment of human health and environmental effects.

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

(iii) Pending the adoption of internationally accepted guidelines, the information required must be generated using available test guidelines accepted by the competent authority (*e.g.* US EPA guideline [54]); where appropriate test guidelines described in Annex II, Part A, should be adapted such that they are appropriate for micro-organisms. Testing should include viable and, if appropriate, non-viable micro-organisms, and a blank control.

(iv) Where testing is carried out, a detailed description (specification) of the material used and its impurities, in accordance with the provisions of point 1.4 of Section 1, must be provided. The material used should be of that specification that will be used in the manufacture of preparations to be authorized.

[54] US EPA Microbial pesticide test guidelines, OPPTS Series 885, February 1996 (http://www.epa.gov/oppbppd1/biopesticides/guidelines/series885.htm)

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

(v) Where the micro-organism has been genetically modified, as defined in Council Directive 90/220/EEC of 23 April 1990 on the deliberate release into the environment of genetically modified organisms [55], a copy of the assessment of risk to the environment conducted in accordance with the provisions of Parts A, B and D and the relevant provisions of Part C, as provided for in Directive 90/220/EEC, must be submitted.

(vi) Where relevant, data must be analysed using appropriate statistical methods. Full details of statistical analysis conducted must be reported (*e.g.* all point estimates must be given with confidence intervals, exact p-values must be given rather than stating significant/non significant).

(vii) In the case of studies in which dosing extends over a period, dosing should preferably be done using a single batch of the micro-organism, if stability permits.

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

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

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

[55] O.J. No. L117/15 8/5/1990

1 Identity of the micro-organism

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

1.1 *Applicant*

The name and address of the applicant (permanent community address) must be provided, as must the name, position, telephone and telefax number of the appropriate person to contact.

Where, in addition, the applicant has an office, agent or representative in the territory of the State, the name and address of the local office, agent or representative must be provided, as must the name, position, telephone and telefax number of the appropriate person to contact.

1.2 *Producer*

The name and address of the producer or producers of the micro-organism must be provided as must the name and address of each plant in which the micro-organism is produced. A contact point (preferably a central contact point, to include name, telephone and telefax number) must be provided, with a view to providing updating information and responding to queries arising, regarding production technology, processes and the quality of product (including where relevant, individual batches).

Where, following inclusion of the micro-organism in Annex I, there are changes in the location or number of producers, the information required must again be notified to the Commission and the Member States.

1.3 *Name and species description, strain characterization*

(i) The micro-organism must be deposited at an internationally recognized culture collection and have been given an accession number, details of which must be submitted.

(ii) Each micro-organism that is subject of an application must be identified and named at the species level. The scientific name and taxonomic grouping, *i.e.* family, genus, species, strain, serotype, pathovar or any other denomination relevant to the micro-organism, must be stated.

In relation to the micro-organism, an indication must be provided as to -

- whether it is indigenous or non-indigenous at the species level to the intended area of application,
- it is a wild type,
- it is a spontaneous or induced mutant, or
- it has been modified, using techniques described in Annex IA Part 2 and Annex IB of Directive 90/220/EEC.

In the latter 2 cases, all known differences between the modified micro-organism and the parent wild strain must be provided.

(iii) Best available technology must be used to identify and characterize the micro-organism at the strain level. The appropriate test procedures and criteria used for identification (*e.g.* morphology, biochemistry, serology, molecular identification) must be reported.

(iv) The common name or alternative and superseded names and code names used during the development, if any, must be provided.

(v) Relationships to known pathogens must be indicated

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

1.4.1 *Content of the micro-organism*

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

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

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

Ideally the plant protection product should be free of contaminants (including contaminating micro-organisms). The acceptability of contaminants, their content and nature should be judged on the basis of a risk assessment conducted by the competent authority.

Where possible and appropriate, the identity and maximum content of all contaminating micro-organisms, expressed in appropriate units, must be reported. Information concerning identity must be provided where possible as specified in point 1.3.

Relevant metabolites (*i.e.* of concern from a human health and/or environmental perspective) formed by the micro-organism must be identified and characterized at different states or growth stages of the micro-organism (*cf* point (viii) of the Introduction)

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

In the case of chemical impurities that are relevant from a human health and/or the environmental perspective, their identity and maximum content, expressed in appropriate terms, must be provided.

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

Information on the identity of chemical substances such as additives must be provided in the form specified in point 1.10 of Part A of this Annex II.

1.4.3 *Analytical profile of batches*

Where relevant, data as specified in point 1.10 of Part A of this Annex II must be reported, using appropriate units.

2 Biological properties of the micro-organism

2.1 *History of the micro-organism and its uses, natural occurrence and geographical distribution*

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

2.1.1 *Historical background*

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

2.1.2 *Origin and natural occurrence*

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

In the case of a mutant, or a genetically modified micro-organism (as defined in Annex IA Part 2 and Annex IB of Directive 90/220/EEC), detailed information must be provided on its production and isolation and on the means by which it can be clearly distinguished from the parent wild strain.

2.2 *Information on target organism(s)*

2.2.1 *Description of the target organism(s)*

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

2.2.2 *Mode of action*

The principal mode of action of the micro-organism must be indicated. Where relevant, it must be reported whether or not the micro-organism produces a toxin with a residual effect on the target organism. Where a toxin is produced, the mode of action of the toxin must be described.

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

The means by which uptake of the micro-organism, or its metabolites (especially toxins) may occur (*e.g.* contact, stomach, inhalation) must be described. It must also be indicated whether or not the micro-organism or its metabolites are translocated in plants and, where relevant, whether such translocation is apoplastic or symplastic or both.
In case of pathogenic effects on the target organism, the infective dose (the dose needed to cause infection with the intended effect on a target species) and the transmissibility (possibility of spread of the micro-organism in the target population, and also from one target species to another (target) species) after application under the proposed condition of use must be reported.

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

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

Details of any experience of toxic effects of the active substance or its metabolic products on humans or animals must be reported. Available information indicating whether the organism is capable of colonizing or invading humans or animals (including immunosuppressed individuals) and whether it is pathogenic must be provided. Details must be provided of any experience concerning the active substance or its products indicating that it may irritate skin, eyes or respiratory organs of humans or animals or indicating that it is allergenic in contact with skin or when inhaled.

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

Information must be presented in relation to the life cycle of the micro-organism, including information concerning symbiosis, parasitism, competitors, predators, host organisms, *etc.*, as well as vectors for viruses.

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

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

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

2.5 ***Infectivity, dispersal and colonization ability***

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

The environmental requirements (temperature, pH, humidity, nutrition requirements, *etc*.) for survival, reproduction, colonization, damage (including human tissues) and effectiveness of the micro-organism must be reported. The presence of specific virulence factors should be indicated.
The temperature range at which the micro-organism grows must be determined, including minimum, maximum and optimum temperatures. This information is of particular value as a trigger for studies on effects on human health (*cf* Section 5).

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

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

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

The possible existence of one or more species of the genus of the active and/or, where relevant, contaminating micro-organisms known to be pathogenic to humans, animals, crops or other non-target species and the type of disease caused by them must be indicated. It must be reported whether or not it is possible, and if so, by which means the active micro-organism can be clearly distinguished from the pathogenic species.

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

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

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

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

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

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

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

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

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

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

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

3 Further information on the micro-organism

Introduction

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

(ii) The information provided must include a detailed description of the normal methods and precautions to be followed in the handling, storage and transport of the micro-organism.

(iii) The studies, data and information submitted, must demonstrate the suitability of the measures proposed for use in emergency situations.

(iv) The information and data listed are required for each micro-organism, except where otherwise specified.

3.1 *Function*

Biological function must be specified from among the following:

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

3.2 *Field of use envisaged*

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

Field use
- Agriculture
- Horticulture
- Forestry
- Viticulture

Protected crops

Amenity

Weed control on non-cultivated areas

Home gardening

House plants

Plant products storage practice

Other (specify)

3.3 *Crops or products protected or treated*

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

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

Full information of the production methods used to manufacture bulk quantities of the micro-organism must be provided.

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

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

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

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

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

Methods to prevent loss of virulence of starting cultures must be developed and be reported.

In addition, any available method that could prevent the micro-organism from losing its effects on the target species must be described.

3.7 ***Recommended methods and precautions concerning handling, storage, transport or fire***

A Safety Data Sheet similar to that required for chemical active substances pursuant to the provisions of Article 27 of the Directive of 1967 must be provided for each micro-organism.

3.8 ***Procedures for destruction or decontamination***

In many cases the preferred or sole means of safe disposal of micro-organisms, contaminated materials, or contaminated packaging, are through controlled incineration in a licensed incinerator.
Methods to dispose safely of the micro-organism or, where necessary, to kill it prior to disposal, and methods to dispose of contaminated packaging and contaminated materials, must be fully described. Data must be provided for such methods to demonstrate their effectiveness and safety.

3.9 ***Measures in case of an accident***

Information on procedures for rendering the micro-organism harmless in the environment (*e.g.* water or soil) in case of an accident must be provided.

4 Analytical methods

Introduction

The provisions of this section only cover analytical methods required for post-registration control and monitoring purposes.

Post-registration monitoring might be considered for all areas of risk assessment. This is particularly the case for (strains of) micro-organisms that are non-indigenous to the intended area of application. A justification demonstrating the validity and suitability of analytical methods used for generation of data as required in accordance with this Annex or for other purposes must be provided; where necessary separate guidance will be developed for such methods on the basis of the requirements specified for methods for post-registration control and monitoring purposes.

Descriptions of methods provided must include details of equipment, materials and conditions used. The applicability of any internationally recognized method must be reported.

As far as practicable methods proposed must employ the simplest approach possible, involve the minimum cost, and require commonly available equipment.

Data on specificity, linearity, accuracy and repeatability, as defined in points 4.1 and 4.2 of Part A of this Annex, are also required for methods used to analyse micro-organisms and their residues.

For this Section the following definitions apply -

impurities	any component (including contaminating micro-organisms and/or chemical substances) other than the specified micro-organism, originating from the manufacturing process or from degradation during storage;
relevant impurities	impurities that are of concern for human or animal health and/or for the environment;
metabolites	metabolites include products resulting from degradative and biosynthetic reactions taking place within the micro-organism or other organisms used to produce the micro-organism of interest,
relevant metabolites	metabolites that are of concern for human or animal health and/or for the environment;
residues	viable micro-organisms and substances produced in significant quantities by these micro-organisms that persist after the disappearance of the micro-organisms and are of concern for human or animal health and/or the environment.

On request the following samples must be provided -

(i) samples of the micro-organism as manufactured,

(ii) analytical standards of relevant metabolites (especially toxins) and all other components included in the residue definition, and

(iii) if available, samples of reference substances for the relevant impurities.

4.1 ***Methods for the analysis of the micro-organism as manufactured***

- Methods for the identification of the micro-organism,
- Methods for providing information on possible variability of seed stock/active micro-organism,
- Methods to differentiate a mutant of the micro-organism from the parent wild strain,
- Methods for the establishment of purity of seed stock from which batches are produced and methods to control that purity;
- Methods to determine the content of the micro-organism in the manufactured material used for the production of formulated products and methods to show that contaminating micro-organisms are controlled to an acceptable level,
- Methods for the determination of relevant impurities in the manufactured material,
- Methods to control the presence of and to quantify (with appropriate limits of determination) the possible presence of any human and mammalian pathogens.
- Methods to determine storage stability and shelf-life of the micro-organism, if appropriate.

4.2 ***Methods to determine and quantify residues (viable or non-viable)***

- of the active micro-organism(s),
- of relevant metabolites (especially toxins),

on and/or in crop, in foodstuffs and feeding stuffs, in animal and human body tissues and fluids, in soil, in water (including drinking water, ground water and surface water) and in air, where relevant.

Analytical methods for amount or activity of proteinaceous products should also be included, *e.g.* by testing exponential cultures and culture supernatants in an animal cell bioassay.

5 **Effects on human health**

Introduction

(i) Available information based on the properties of the micro-organism and corresponding organisms (point 1-3), including health and medical reports may be sufficient for a decision as to whether or not the micro-organism would cause health effects (infectious/pathogenic/toxic) in humans.

(ii) The information provided, taken together with that provided for one or more preparations containing the micro-organism, must be sufficient to permit an evaluation to be made as to the risks for man, directly and /or indirectly associated with the handling and use of plant protection products containing the micro-organism, the risks for man handling treated products, and the risks for man arising from residual traces or contaminants remaining in food and water. In addition, the information provided must be sufficient to -

- permit a decision to be made as to whether, or not, the micro-organism can be included in Annex I,
- specify appropriate conditions or restrictions to be associated with any inclusion in Annex I,
- specify risk and safety phrases (once introduced) for the protection of man, animals and the environment to be included on packaging (containers);
- identify relevant first aid measures as well as appropriate diagnostic and therapeutic measures to be followed in the event of infection or other adverse effect in man;

(iii) All effects observed during testing and investigation must be reported. Investigations necessary to permit evaluation of the probable mechanism involved, and to assess the significance of observed effects, must be performed.

(iv) For all studies actual achieved dose, expressed in colony forming units per kg body weight (cfu/kg), as well as in other appropriate units, must be reported.

(v) Evaluation of the effects on human health of the micro-organism should be carried out in a tiered manner.

The first tier (Tier I) includes available basic information and basic studies, which must be performed for all micro-organisms. Expert judgment, applied on a case by case basis, is necessary to define the testing regime appropriate for individual micro-organisms. Newly generated data from conventional toxicological and/or pathological experiments on laboratory animals are normally required unless the applicant can demonstrate, on the basis of existing information, that use of the micro-organism, under the proposed conditions of use, does not have any harmful effects on human and animal health. Pending the adoption of internationally accepted guidelines, the information required must be generated using available test guidelines accepted by the competent authority (*e.g.* US EPA guideline).

Tier II studies must be conducted if testing in accordance with Tier I demonstrated potential for adverse health effects. The type of study to be performed depends on the nature of the effects observed in the Tier T testing. Before performing such studies, the applicant must seek agreement of the competent authority on the type of study to be performed.

TIER I

5.1 ***Basic information***

Basic information is required concerning the micro-organism's potential to cause adverse effects such as its ability to colonize, to cause damage and to produce toxins and other relevant metabolites.

5.1.1 *Medical data*

Where available, and without prejudice to the provisions of Article 5 of Council Directive 80/1107/EEC of 27 November 1980 on the protection of workers from the risks related to chemical, physical and biological agents at work and Articles 5 to 17 of Council Directive 90/679/EEC of 26 November 1990 on the protection of workers from the risks related to biological agents at work [56], practical information and data concerning the recognition of the symptoms of infection or pathogenicity and concerning the effectiveness of first aid and therapeutic measures must be submitted. The effectiveness of potential antagonists should be investigated and be reported. Where relevant, methods to kill or render the micro-organism non-infective must be indicated (*cf* point 3.8).

Data and information concerning the effects of human exposure, where available and of the necessary quality, are of particular value, in confirming the validity of extrapolations made on the basis of testing using laboratory animals, as well as conclusions reached with respect to target organs, virulence, and the reversibility of adverse effects. Such data can be generated following accidental or occupational exposure.

5.1.2 *Medical surveillance on manufacturing plant personnel*

Available reports of occupational health surveillance programmes, supported with detailed information on the design of the programmes and on exposure to the micro-organism must be submitted. Such reports should, where feasible, include data relevant to the mechanism of action of the micro-organism. These reports shall, where available, include data from persons exposed in manufacturing plants or after application of the micro-organism (*e.g.* in efficacy trials).

Special attention should be given to those whose susceptibility may be affected, *e.g.* because of pre-existing disease, medication, compromised immunity, pregnancy or breast feeding.

5.1.3 *Sensitisation/allergenicity observations, if appropriate*

Available information on the sensitisation and allergenic response of workers, including workers in manufacturing plants, agricultural and research workers and others exposed to the micro-organism must be provided, and include, where relevant, details of any incidences of hypersensitivity and chronic sensitisation. The information provided must include available information concerning frequency, level and duration of exposure, symptoms observed and other relevant clinical observation. Information should be included as to whether or not workers were subjected to any allergy tests or interviewed about allergenic symptoms.

[56] O.J. No L374/1 31/12/1990

5.1.4 *Direct observation, e.g. clinical cases*

Available reports from the open literature, relating to clinical cases and poisoning incidents involving the micro-organism or closely related members of the taxonomic group, where they are from refereed journals or official reports, must be submitted together with reports of any follow-up studies undertaken. Such reports are of particular value and should contain complete descriptions of the nature, level and duration of exposure, as well as the clinical symptoms observed, first aid and therapeutic measures applied and measurements and observations made. Summary and abstract information is of limited value.

Where animal studies are performed, reports relating to clinical cases can be of particular value in confirming the validity of extrapolations from animal data to man and in identifying unexpected adverse effects that are specific to humans.

5.2 ***Basic studies***

To facilitate correct interpretation of test results, it is of greatest importance that the test methods used be appropriate in relation to species sensitivity, administration route *etc.*, and relevant from a biological and toxicological perspectives. The route of administration of the test micro-organism should reflect the main exposure routes for humans.

To evaluate medium - and long-term effects following acute, sub-acute or semi-chronic exposure to micro-organisms, it is necessary to avail of the options provided in most of the OECD test guidelines, to extend testing to include a recovery period (after which full macroscopic and microscopic pathology is to be performed, including an exploration for micro-organisms in tissues and organs). Such extended testing facilitates the interpretation of certain effects and provides the opportunity to recognize infectivity and/or pathogenicity, which in turn facilitates decision-making on other issues such as the necessity to perform long term studies (*e.g.* carcinogenicity, (point 5.3) and residues studies (point 6.2)).

5.2.1 *Sensitisation* [57]

Aim of the test

The test will provide sufficient information to assess the potential of the micro-organism to provoke sensitisation reactions by inhalation as well as following dermal exposure. A maximization test must be performed.

[57] Available methods for testing dermal sensitisation are not suitable for testing micro-organisms. Sensitisation by inhalation is most probably a greater problem than dermal exposure in the case of micro-organisms but, there are no validated test methods available at present. Development of such methods is important. Until such methods become available, all micro-organisms should be regarded as being potential sensitisers. This approach takes into consideration immuno-compromised or other sensitive individuals in the population (*e.g.* pregnant women, new-born children or elderly).

Circumstances in which required [58]

Information on sensitisation must be reported.

5.2.2 *Acute toxicity, pathogenicity and infectivity*

The studies, data and information to be provided and evaluated must be sufficient to permit the identification of effects following a single exposure to the micro-organism, and in particular to establish, or indicate -

- the toxicity, pathogenicity and infectivity of the micro-organism,
- the time course and characteristics of the effects with full details of behavioural changes and possible gross pathological findings at post-mortem,
- where possible mode of toxic action,
- the relative hazard associated with the different routes of exposure, and
- the clearance of the micro-organism though blood analyses conducted throughout the studies.

Infectivity and/or more long-term effects that cannot be observed immediately may accompany acute toxic/pathogenic effects. With a view to the evaluation of possible health effects, it is therefore necessary to carry out studies on the ability of the micro-organism to infect following administration by the oral and inhalation routes and following intraperitoneal/subcutaneous injection of test mammals.

During the acute toxicity, pathogenicity and infectivity studies conducted, an estimation must be made of the clearance of the micro-organism and/or the active toxin in organs deemed to be relevant for microbial examination (*e.g.* liver, kidneys, spleen, lungs, brain, blood and site of administration). The observations to be made should reflect expert scientific judgement and may include -

- micro-organism numeration in all the tissues likely to be affected (*e.g.* showing lesions) and in the main organs: kidneys, brain, liver, lungs, spleen, bladder, blood, lymphatic ganglia, gastro-intestinal tract, thymus gland ,
- and lesions at the inoculation site in dead or moribund animals and at interim and final sacrifice.

The information generated through acute toxicity, pathogenicity and infectivity testing is of particular value in assessing hazards likely to arise in accident situations and in assessing consumer risks due to exposure to residues.

[58] In the absence of agreed and internationally validated test methods all micro-organisms will be labelled as potential sensitisers, unless applicants demonstrate non-sensitising potential by means of data submitted. Accordingly this data requirement must be regarded as not being obligatory, rather it is optional, but on a provisional base.

5.2.2.1 *Acute oral toxicity, pathogenicity and infectivity*

Circumstances in which required

The acute oral toxicity, pathogenicity and infectivity of the micro-organism must be reported.

5.2.2.2 *Acute inhalation toxicity, pathogenicity and infectivity*

Circumstances in which required

The inhalation toxicity [59], pathogenicity and infectivity of the micro-organism must be reported.

5.2.2.3 *Intraperitoneal/Subcutaneous single dose*

An intraperitoneal/subcutaneous test is considered a highly sensitive assay to assess in particular infectivity.

Circumstances in which required

The intraperitoneal route is in principle required for all micro-organisms, however expert judgement may be exercised in deciding whether subcutaneous injection is preferred instead of intraperitoneal injection where the maximum temperature for growth and multiplication is lower than 37 °C.

5.2.3 *Genotoxicity testing*

Circumstances in which required

If exotoxins are produced by the micro-organism (*cf* point 2.8), those exotoxins and any other relevant metabolites in the culture medium must be tested for genotoxicity. Where possible testing should be carried out using purified toxins and metabolites.

Where, on the basis of expert judgement and having regard to the relevance and validity of the data available, it is concluded that there is no evidence that toxic metabolites are formed, testing on the micro-organism itself must be considered. In the case of viruses the risk of insertional mutagenesis in mammal cells or the risk of carcinogenicity must be considered.

Aim of the test

These studies are of value in -

- the prediction of genotoxic potential,
- the early identification of genotoxic carcinogens, and
- the elucidation of the mechanism of action of some carcinogens.

[59] An inhalation study may be replaced by an intratracheal study.

It is important that a flexible approach is adopted, with selection of further tests being dependent upon interpretation of results at each stage.

Test conditions [60]

The genotoxicity potential of cellular micro-organisms should, whenever possible, be studied using broken cells. A justification must be provided as to the suitability of the method of sample preparation used

In the case of viruses infectious isolates must be used for testing.

5.2.3.1 *In vitro studies*

Circumstances in which required

In vitro mutagenicity tests (bacterial assay for gene mutation, test for clastogenicity in mammalian cells and test for gene mutation in mammalian cells) must be provided.

5.2.4 *Cell culture study*

A cell culture study must be reported for intracellular replicating micro-organisms, such as viruses, viroids or specific bacteria and protozoa, unless the information provided in accordance with Sections 1 to 3 clearly demonstrate that the micro-organism does not replicate in warm blooded organisms. The study should be performed using human cell or tissue cultures of different organs. Selection can be based on expected target organs following infection. Where human cell or tissue cultures of specific organs are not available, other mammalian cell and tissue cultures can be used. In the case of viruses, ability to interact with the human genome is a key consideration.

5.2.5 *Information on short-term toxicity and pathogenicity*

Aim of the test

Short-term toxicity studies must be designed to provide information as to the amount of the micro-organism that can be tolerated without toxic effects under the conditions of the study. Such studies provide useful data on the risks for those handling and using preparations containing the micro-organism. In particular, short-term studies provide an essential insight into possible cumulative effects of the micro-organism, and the risks to workers who may be exposed over extensive periods. In addition short-term studies provide information useful in the design of chronic toxicity studies.
The studies, data and information to be provided and evaluated, must be sufficient to permit the identification of effects following repeated exposure to the micro-organism, and in particular to further establish, or indicate -

- the relationship between dose and adverse effects,
- the toxicity of the micro-organism including where possible the NOAEL for toxins,
- the target organs, where relevant,

[60] As the current test methods are designed for use with soluble chemicals, it is necessary that they be further developed for testing of micro-organisms.

- the time course and characteristics of the effects with full details of behavioural changes and possible gross pathological findings at post-mortem,
- specific toxic effects and pathological changes produced,
- where relevant the persistence and reversibility of certain toxic effects observed, following discontinuation of dosing,
- where possible, the mode of toxic action, and
- the relative hazard associated with the different routes of exposure.

During short-term toxicity testing, an estimation must be made of the clearance of the micro-organism clearance in the main organs.

Pathogenicity and infectivity end points must be investigated and be reported

Circumstances in which required

The short-term toxicity (minimum 28 days) of the micro-organism must be reported.

The choice of test species must be justified. A decision concerning study duration should reflect acute toxicity and clearance data.

Expert judgement is required to decide the route of administration that is appropriate in individual cases.

5.2.5.1 *Health effects after repeated inhalation exposure*

Information on health effects following repeated exposure by the inhalation route is necessary, particularly for risk assessment in relation to occupational situations. Repeated exposure can influence the clearance capacity (*e.g.* resistance) of the host (human). Furthermore, toxicity following repeated exposure to contaminants, growth medium, co-formulants and the micro-organism must be addressed to facilitate proper risk assessment. It must be appreciated that formulants in the plant protection product can influence the toxicity and infectivity of a micro-organism.

Circumstances in which required.

Information on the short-term infectivity, pathogenicity and toxicity by the inhalation route is required, unless the information otherwise provided is sufficient to permit assessment of human health effects. This can be the case where it is demonstrated that the test material has no inhalable fraction and/or repeated exposure is not expected.

5.2.6 *Proposed treatment: first aid measures, medical treatment*

The first aid measures to be used in the event of infection and in the event of contamination of eyes must be provided.

Therapeutic regimes for use in the event of ingestion or contamination of eyes and skin must be described in full. Information based on practical experience, where it exists and is available, in

other cases on theoretical grounds, as to the effectiveness of alternative treatment regimes, where relevant, must be provided.

Information on resistance to antibiotics must be provided.

{END OF TIER I}

TIER II

5.3 ***Specific toxicity, pathogenicity and infectivity studies***

In certain cases, it is necessary to carry out supplementary studies to further clarify adverse human health effects.

In particular, where the results of Tier I testing indicate that the micro-organism may lead to long-term health effects, studies on chronic toxicity, pathogenicity and infectivity, carcinogenicity and reproductive toxicity must be carried out. Where a toxin is produced, toxicokinetic studies must be performed.

Testing programmes must be designed on a case by case basis, in the light of the particular parameters to be investigated and the objectives to be achieved. Before conducting such studies, the applicant must seek the agreement of the competent authority on the type of studies to be performed.

5.4 ***In vivo studies in somatic cells***

Circumstances in which required

If all the results of the *in vitro* studies are negative further testing must be done, taking into consideration all other relevant information available (including toxicokinetic, toxicodynamic and physico-chemical data and data on analogous micro-organisms, toxins and metabolites). The test can be an *in vivo* study or an *in vitro* study using a different metabolising system from that/those previously used.

If the *in vitro* cytogenetic test is positive, an *in vivo* test using somatic cells (metaphase analysis in rodent bone marrow or micronucleus test in rodents) must be conducted.

If either of the *in vitro* gene mutation tests is positive, an *in vivo* test to investigate unscheduled DNA synthesis or a mouse spot test must be conducted.

5.5 ***Genotoxicity - In vivo studies in germ cells***

Circumstances in which required

When any result of an *in vivo* study in somatic cells is positive, *in vivo* testing for germ cell effects may be justified. The necessity for conducting these tests will have to be considered on a case by case basis, taking into account information regarding toxicokinetics, use and anticipated exposure. Suitable tests involve interaction with DNA (such as the dominant lethal assay), to assess the potential for inherited effects and possibly make a quantitative assessment of heritable effects. It is recognised that in view of their complexity, the use of quantitative studies requires strong justification.

{END OF TIER II}

5.6 ***Summary of mammalian toxicity, pathogenicity and infectivity and overall evaluation.***

A summary of all data and information provided in accordance with paragraphs 5.1 through 5.5, must be submitted, and include a detailed and critical assessment of those data in the context of relevant evaluative and decision making criteria and guidelines, with particular reference to the risks for man and animals that may or do arise, and the extent, quality and reliability of the data base.

The summary must include an assessment as to whether or not exposure of animals or humans has any implications for vaccination or serological monitoring

6 Residues in or on treated products, food and feed

Introduction

(i) The information provided, taken together with that for one or more preparations containing the micro-organism, must be sufficient to permit an evaluation to be made as to the risk for man and/or animals, arising from exposure to residual traces of the micro-organism and metabolites (toxins) remaining in or on plants or plant products.

(ii) In addition, the information provided must be sufficient to:

- permit a decision to be made as to whether or not the micro-organism can be included in Annex I,
- specify appropriate conditions or restrictions to be associated with any inclusion in Annex I,
- where relevant, set maximum residue levels, pre-harvest intervals to protect consumers and waiting periods to protect workers handling treated crops and products.

(iii) Experimental data on levels of exposure to residues may not be required where a justification is provided, demonstrating that the micro-organism and its metabolites do not present risks to the health of consumers in the concentrations that could occur as a consequence of authorized use. Such a justification can be based upon open literature information, practical experience and information submitted in accordance with Sections 1, 2, 3 and 5.

6.1 *Persistence and likelihood of multiplication in or on crops, feedingstuffs or foodstuffs*

A quantitative estimate of the persistence/competitiveness of the micro-organism and relevant secondary metabolites (especially toxins) in or on treated crops of plant products under the environmental conditions prevailing at and after the intended use, taking into account in particular the information provided in Section 2, must be provided.

In addition, a statement must be provided indicating the extent and basis on which it is considered that the micro-organism can (or cannot) multiply in or on plants or plant products or during processing of raw products.

6.2 *Further information required*

Since consumers may be exposed to micro-organisms for a considerable time as a result of consumption of treated food commodities; a toxicological endpoint for risk management purposes, such as the ADI, must be established on the basis of chronic or semi-chronic studies.

6.2.1 *Non-viable residues*

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

If the micro-organism or metabolites produced by it, especially toxins, are persistent (*cf* points 2.4 and 2.5), full experimental residue data as provided for in Section 6 of Part A, must be provided, where the concentrations of the micro-organism and/or its toxins in or on the treated foodstuffs or feedingstuffs are expected to occur -

- in concentrations higher than under natural conditions, or
- in a different phenotypic state.

Conclusions concerning natural concentrations and elevated concentration due to treatment with the micro-organism, must be based on experimental data, and not on extrapolations or calculations made using models.

Before performing such studies, the applicant must seek the agreement of the competent authority on the type of studies to be performed.

6.2.2 *Viable residues*

If the information submitted in accordance with point 6.1, is indicative of relevant amounts of the micro-organism in or on treated products, food or feed, being persistent, possible effects on humans and/or animals must be investigated, unless it can be justified on the basis of the information and data provided in accordance with Section 5, that the micro-organism and its metabolites and/or degradation products do not have harmful effects on humans in the concentrations and form that could occur as a result of authorised use.

Conclusions concerning natural concentrations and elevated concentration due to treatment with the micro-organism, must be based on experimental data, and not on extrapolations or calculations made using models.

Particular attention to the persistence of viable residues is necessary where infectivity or pathogenicity to mammals occur (*cf* points 2.3 and 2.5 and Section 5) and/or if any other information suggests a hazard to consumers and/or workers. In such cases, the competent authority may require submission of studies similar to those provided for in Part A of this Annex.

Before performing such studies, the applicant must seek the agreement of the competent authority on the type of studies to be performed.

6.3 ***Summary and evaluation of residue behaviour resulting from data submitted in accordance with points 6.1 and 6.2.***

7 Fate and behaviour in the environment

Introduction

(i) Information on the origin, properties, and survival of the micro-organism and its residual metabolites as well as its intended use form the basis for an assessment of environmental fate and behaviour.

Experimental data are required unless a justification is provided demonstrating that an assessment of fate and behaviour in the environment can be completed on the basis of existing information. Justifications can be based on information and data in the open literature, on practical experience and, on information provided in accordance with the requirements specified in Sections 1 through 6. The origin and natural occurrence of the micro-organism (*cf* point 2.1.2) is of particular relevance in preparing such justifications.

(ii) The information provided, taken together with other relevant information, and that for one or more preparations containing the micro-organism, must be sufficient to permit an assessment of its fate and behaviour as well as that of its residual traces and toxins, where they are of significance for human health and/or the environment.

(iii) In particular, the information provided for the micro-organism, together with other relevant information, and that for one or more preparations containing the micro-organism should be sufficient -

- to decide whether, or not, the micro-organism can be included in Annex I,
- to specify appropriate conditions or restrictions to be associated with any inclusion in Annex I,
- to specify the hazard symbols, the indications of danger, and relevant risk and safety phrases for the protection of the environment, which are to be included on packaging (containers),
- to predict the distribution, fate, and behaviour in the environment of the micro-organism and its metabolites as well as the time courses involved,
- to identify non-target species and populations for which hazards arise because of potential exposure, and
- to identify measures necessary to minimize contamination of the environment and impact on non-target species.

(iv) Relevant metabolites (*i.e.* of concern for human health and/or the environment) formed by the test organism under relevant environmental conditions must be characterised. Where relevant metabolites are present in or produced by the micro-organism, data as specified in Section 7 of Part A of this Annex may be required, where the following conditions are met -

- the relevant metabolite is stable outside the micro-organism (*cf* point 2.8), and
- a toxic effect produced by the relevant metabolite occurs in the absence of the micro-organism, and
- the relevant metabolite is likely to occur in the environment in concentrations considerably higher than under natural conditions.

(v) Available information concerning relationship to naturally occurring wild type relatives must be taken into account.

(vi) Before undertaking studies as referred to hereunder, the applicant must seek the agreement of the competent authority on the need for such studies and on their design. Information generated in accordance with other Sections of this Annex must also be taken into account.

7.1 ***Persistence and multiplication***

Information on the persistence and multiplication of the micro-organism, in all relevant environmental compartments must be provided, unless a justification has been submitted demonstrating that exposure of the particular environmental compartment to the micro-organism is unlikely to occur. Special attention must be given to -

- competitiveness under the environmental conditions prevailing at and after the intended use, and
- population dynamics in seasonally or regionally extreme climates (particularly hot summer, cold winter and rainfall) and to agricultural practices applied after intended use.

Estimates of the levels of the micro-organism occurring over time, following use of the product under the proposed conditions of use, must be provided.

7.1.1 *Soil*

Information on viability/population dynamics must be reported for several cultivated and non-cultivated soils representative of the range of soils in the various Community regions where use exists or is anticipated. The provisions on choice of soil and its collection and handling, specified in point 7.1 of Part A of this Annex, must be followed. If the test organism is to be used in association with other media (*e.g.* rockwool), this must be included in the testing regimen.

7.1.2 *Water*

Information on viability/population dynamics in natural sediment/water systems under both dark and illuminated conditions must be reported.

7.1.3 *Air*

Where there are particular concerns in relation to operator, worker or bystander exposure, information on the concentrations in air may be required.

7.2 ***Mobility***

The possible movement of the micro-organism and its degradation products into other environmental compartments must be evaluated, unless a justification is submitted demonstrating that exposure of the environmental compartments concerned to the micro-organism is unlikely to occur. Such justifications may include information concerning the intended use (*e.g.* field or greenhouse, application to soil or to crops), life cycle stages, including occurrence of vectors, persistence and the ability of the organism to colonise adjacent habitats.

Particular attention must be paid to the spread, the persistence and probable transport ranges of the micro-organism where toxicity, infectivity or pathogenicity have been reported or if any

other information suggests possible hazard to humans, animals or to the environment. In such cases the competent authority may require studies similar to specified in Part A of this Annex to be conducted and reported. Before undertaking such studies, the applicant must seek the agreement of the competent authority on the type of studies to be performed.

8 **Effects on non-target organisms**

Introduction

(i) The information provided in accordance with the preceding Sections – identity of the micro-organism, biological properties, further information, analytical methods, effects on human health, residues in or on treated products, food or feed, fate and behaviour in the environment - is central to the assessment of impact on non-target species.

Experimental data are normally required, unless a justification is provided demonstrating that an assessment of effects on non-target organisms can be performed on the basis of the information already available.

(ii) The choice of non-target organisms made for testing to identify and quantify environmental effects should reflect the identity of the micro-organism (including the host specificity, mode of action and ecology of the organism). On the basis of that information it should be possible to choose appropriate test-organisms, such as organisms closely related to the target organism.

(iii) The information provided, taken together with that for one or more preparations containing the micro-organism, must be sufficient to permit an assessment of the impact on non-target species (flora and fauna), likely to be at risk from exposure to the micro-organism, where they are of environmental significance. Impact can result from single, prolonged or repeated exposure and can be reversible or irreversible.

(iv) In particular, the information provided for the micro-organism, together with other relevant information, and that provided for one or more preparations containing it, should be sufficient to -

- decide whether, or not, the micro-organism can be included in Annex I,
- specify appropriate conditions or restrictions to be associated with any inclusion in Annex I,
- permit an evaluation of short and long term risks for non-target species - populations, communities, and processes - as appropriate,
- classify the micro-organism as to biological hazard,
- specify the precautions necessary for the protection of non-target species, and
- specify the hazard symbols, the indications of danger, and relevant risk and safety phrases for the protection of the environment, to be mentioned on packaging (containers).

(v) There is a need to report all potentially adverse effects found during routine ecotoxicological investigations and to undertake and report, where required by the competent authority, such additional studies that may be necessary to investigate the probable mechanisms involved and to assess the significance of these effects. All available biological data and information that are relevant to the assessment of the ecotoxicological profile of the micro-organism must be reported.

(vi) For all studies, average achieved dose in cfu/kg body weight as well as in other appropriate units must be reported.

(vii) It may be necessary to conduct separate studies for relevant metabolites (especially toxins), where these products can constitute a relevant risk to non-target organisms and where their effects cannot be evaluated on the basis of available results relating to the micro-organism. In assessing the need for such studies, consideration must be given to the information provided in accordance with the provisions of Sections 5, 6 and 7 must be taken into account. Before such

studies are performed, the applicant must seek agreement of the competent authority as to whether or not such studies and required and with regard to their design.

(viii) In order to facilitate the assessment of the significance of test results obtained, including the estimation of intrinsic toxicity, infectivity and pathogenicity and the factors affecting toxicity, infectivity and pathogenicity, the same strain (or recorded origin) of each relevant species should, where possible, be used in the various tests specified.

(ix) Tests must be performed unless a justification is provided demonstrating that the non-target organism will not be exposed to the micro-organism. Where it is established that the micro-organism does not cause toxic effects or is not pathogenic or infective to vertebrates or plants, only reaction to appropriate non-target organisms must be investigated.

8.1 ***Effects on birds***

Aim of the test

Information on toxicity, infectivity and pathogenicity to birds must be reported.

8.2 ***Effects on aquatic organisms***

Aim of the test

Information on toxicity, infectivity and pathogenicity to aquatic organisms must be reported.

8.2.1 *Effects on fish*

Aim of the test

Information on toxicity, infectivity and pathogenicity to fish must be reported.

8.2.2 *Effects on freshwater invertebrates*

Aim of the test

Information on toxicity, infectivity and pathogenicity to freshwater invertebrates must be reported.

8.2.3 *Effects on algae growth*

Aim of the test

Information on effects on algal growth, growth rate and capacity to recover must be reported.

8.2.4 *Effects on plants other than algae*

Aim of the test

Information on effects on plants other than algae must be reported.

8.3 ***Effects on bees***

Aim of the test

Information on toxicity, infectivity and pathogenicity to bees must be reported.

8.4 ***Effects on arthropods other than bees***

Aim of the test

Information on toxicity, infectivity and pathogenicity to arthropods other than bees must be reported. The choice of test species should reflect the potential use of plant protection products containing the micro-organism (*e.g.* foliar or soil application). Particular attention should be given to organisms used for biological control and organisms playing an important role in integrated pest management (IPM).

8.5 ***Effects on earthworms***

Aim of the test

Information on toxicity, infectivity and pathogenicity to earthworms must be reported.

8.6 ***Effects on non-target soil micro-organisms***

Impact on relevant non-target micro-organisms and on their predators (*e.g.* protozoa for bacterial inoculants) must be reported. Expert judgement is necessary to decide whether or not additional studies are necessary. Due consideration should be given to data and information provided in accordance with this and other Sections, in particular data on the specificity of the micro-organism, and expected exposure. Useful information may also be available from observations made in the course of efficacy testing. Particular attention should be given to organisms used in integrated crop management (ICM).

8.7 ***Additional studies***

Additional studies to be conducted and reported might include further acute studies using additional species or processes (such as sewage systems) or higher tier studies such as chronic, sub-lethal or reproductive studies on selected non-target organisms.

Before performing such studies, the applicant must seek the agreement of the competent authority on the type of studies to be performed.

9 **Summary and evaluation of environmental impact**

A summary and evaluation of all data relevant to environmental impact, should be carried out in accordance with the guidance documents specified in the **Fourth Schedule**. The summary and evaluation provided should include a detailed and critical assessment of the supporting data in the context of relevant evaluative and decision making criteria and guidelines, having particular regard to risks for the environment and non-target species that may or do arise, and the extent, quality and reliability of the data base.

The following particular issues must be addressed -

- distribution and fate in the environment, and the time courses involved;
- identification of non-target species and populations at risk, and the extent of their potential exposure;
- identification of precautions necessary to avoid or minimise contamination of the environment, and for the protection of non-target species.

10 **Proposals including justification of the proposals for the classification and labelling of the active substance in accordance with the Directive of 1967 -**

- Hazard symbol(s)
- Indications of danger
- Risk phrases
- Safety phrases

11 **A dossier as referred to in Annex III, Part B, for a representative plant protection product**

Appendix 3

Annex III to Directive 91/414/EC

(Annex III to the Directive of 1991, as amended Commission Directive No 93/71/EEC of 27 July 1993, the corrigendum to Commission Directive No 93/71/EEC of 27 July 1993, Commission Directive 94/37/EC of 22 July 1994, Commission Directive 94/79/EC of 21 December 1994, Commission Directive 95/35/EC of 14 July 1995, Commission Directive 95/36/EC of 14 July 1995, Commission Directive 96/12/EC of 8 March 1996, Commission Directive 96/46/EC of 16 July 1996, Commission Directive 96/68/EC of 21 October 1996, and Commission Directive 2001/36/EC of 16 May 2001)

REQUIREMENTS FOR THE DOSSIER TO BE SUBMITTED FOR THE AUTHORIZATION OF A PLANT PROTECTION PRODUCT

INTRODUCTION

The information required shall:

1.1 include a technical dossier supplying the information necessary for evaluating efficacy and the foreseeable risks, whether immediate or delayed, which the plant protection product may entail for humans, animals and the environment and containing at least the information and results of the studies referred to below;

1.2 where relevant, be generated using test guidelines referred to or described in this Annex; in the case of studies initiated before the adoption of the modification of this Annex, the information shall be generated using suitable internationally or nationally validated test guidelines or, in the absence thereof, test guidelines accepted by the competent authority;

1.3 in the event of a test guideline being inappropriate or not described, or where another one than those referred to in this annex has been used, include a justification, which is acceptable to the competent authority for the guidelines used;

1.4 include, a full description of the test guidelines used, except if they are referred to or described in this Annex, and a full description of any deviations from them including a justification, which is acceptable to the competent authority, for these deviations;

1.5 include a full and unbiased report of the studies conducted as well as a full description of them or a justification, which is acceptable to the competent authority where -

- particular data and information which would not be necessary owing to the nature of the product or its proposed uses, are not provided, or
- it is not scientifically necessary, or technically possible to supply information and data.

1.6 where relevant, have been generated in accordance with the requirements of Directive 86/609/EEC.

2.1 Tests and analyses must be conducted in accordance with the principles laid down in Directive 87/18/EEC, where testing is done to obtain data on the properties and/or safety with respect to human health or the environment.

2.2 Tests and analyses, required under the provisions of section 6 points 6.2 to 6.6 of this annex, shall, where they are conducted outside the territory of the State, be conducted by official or officially recognized testing facilities or organisations in the Member State concerned, which satisfy at least the following requirements

- have at their disposal sufficient scientific and technical staff, having the necessary education, training, technical knowledge and experience for their assigned functions,
- have at their disposal suitable items of equipment required for correct performance of the tests and measurements that it claims to be competent to carry out. This equipment shall be properly maintained and calibrated where appropriate before being put into service and thereafter according to an established programme,
- have at their disposal appropriate experimental fields and, where necessary glasshouses, growth cabinets or storage rooms. The environment in which tests are undertaken shall not invalidate its results or adversely effect the required accuracy of measurement,
- make available to all relevant personnel operating procedures and protocols used for the trials,
- make available, where requested by the competent authority, prior to the commencement of a test, detailed information on it, containing at least its location and the plant protection products included in it,
- ensure that the quality of the work performed is appropriate to its type, range, volume and intended purpose,
- maintain records of all original observations, calculations and derived date, calibration records and the final test report as long as the product concerned is authorised in the Community.

2.3 Tests and analyses, required under the provisions of section 6 points 6.2 to 6.6 of this annex, shall, where they are conducted within the territory of the State, be conducted in accordance with the Principles of Good Experimental Practice set out in the Sixth Schedule, or in compliance with Irish/European Standard IS/EN 45001 and in accordance with the authorization for trials or trials permit concerned.

2.4 Notwithstanding the provisions of point 2. 1, tests and analyses started on or before the 31 December 1999 and performed to obtain data on the properties and/or safety with respect to honeybees and beneficial arthropods other than bees, may have been conducted by officially recognized testing facilities or organisations, in accordance with the Principles of Good Experimental Practice laid down in the Sixth Schedule, or in compliance with Irish/European Standard IS/EN 45001, where they are conducted within the territory of the State, and in accordance with the requirements of point 2.2, where they are conducted outside the territory of the State.

2.5 Notwithstanding the provisions of point 2.1, supervised residue trials conducted in accordance with the provisions of Section 8, relating to plant protection products containing active substances already on the market prior to 25 July 1993 and started on or before the 31 December 1997, may have been conducted by officially recognized testing facilities or organisations, in accordance with the Principles of Good Experimental Practice laid down in the Sixth Schedule, or in compliance with Irish/European Standard IS/EN 45001, where they are conducted within the territory of the State, and in accordance with the requirements of point 2.2, where they are conducted outside the territory of the State.

2.6 Notwithstanding the provisions of point 2.1, for active substances consisting of micro-organisms or viruses, tests and analyses done to obtain data on the properties and/or safety with respect to aspects other than human health, may have been conducted by official or officially recognized testing facilities or organisations in accordance with the Principles of Good Experimental Practice laid down in the Sixth Schedule, or in compliance with Irish/European Standard IS/EN 45001, where they are conducted within the territory of the State, and in accordance with the requirements of point 2.2 of the introduction to Annex III, where they are conducted outside the territory of the State.

3 The information required shall include the proposed classification and labelling of the plant protection product in accordance with relevant Community Directives.

4 In individual cases it may be necessary to require certain information as provided for in Annex II, Part A, for formulants. Before such information will be required and before possibly new studies have to be performed, all information on the formulant, made available to the competent authority, shall be considered, in particular when -

- the use of the formulant is permitted in food, animal feeding stuffs, medicines or cosmetics in accordance with Community legislation; or
- a safety data sheet has been submitted for the formulant in accordance with the Directive of 1967.

PART A

Chemical Preparations

1 Identity of the plant protection product

The information provided, taken together with that provided for the active substance(s), must be sufficient to identify preparations, with precision, and to define them in terms of their specification and nature. The information and data referred to, unless otherwise specified, are required for all plant protection products.

1.1 *Applicant (name and address, etc.)*

The name and address of the applicant (permanent community address) must be provided as must the name, position, telephone and telefax number of the appropriate person to contact.

Where, in addition, the applicant has an office, agent or representative in the territory of the State, the name and address of the local office, agent or representative should be provided, as should the name, position, telephone and telefax number of the appropriate person to contact.

1.2 *Manufacturer of the preparation and the active substance(s) (names and addresses, etc. including location of plants)*

The name and address of the manufacturer of the preparation and of each active substance in the preparation must be provided as must the name and address of each manufacturing plant in which the preparation and active substance are manufactured.

A contact point (preferably a central contact point, to include name, telephone and telefax numbers) must be provided for each.

If the active substance originates from a manufacturer from which data according to Annex II had not been submitted previously, a statement of purity and detailed information on the impurities as required in Annex II must be provided.

1.3 *Trade name or proposed trade name, and manufacturer's development code number of the preparation if appropriate*

All former and current trade names and proposed trade names and development code numbers of the preparation as well as the current names and numbers must be provided. Where trade names and code numbers referred to, relate to similar but different preparations (possibly obsolete), full details of the differences, must be provided. (The proposed trade name may not give rise to confusion with the trade names of plant protection products already authorized).

1.4 *Detailed quantitative and qualitative information on the composition of the preparation (active substance(s), and formulant(s)*

1.4.1 For preparations the following information must be reported -

- the content of both technical active substance(s) and pure active substance(s); and
- the content of formulants.

The concentrations must be expressed -

- for preparations that are solids, aerosols, volatile liquids (maximum boiling point 50 °C) or viscous liquids (lower limit 1 PA at 20 °C), as a percentage by weight,
- for other liquids, as a percentage by weight and in grams per litre at 20 °C, and
- for gasses, as a percentage by volume.

1.4.2 For active substances their ISO common names or proposed ISO common names and their CIPAC numbers, and, where available, the EEC (EINECS or ELINCS) numbers must be provided. Where relevant it must be stated which salt, ester, anion or cation is present.

1.4.3 Formulants must where possible, be identified both by their chemical name as given in Annex I to the Directive of 1967, or, if not included in that Directive, in accordance with both IUPAC and CA nomenclature. Their structure or structural formula must be provided. For each component of formulants the relevant EEC (EINECS or ELINCS) number and CAS number where they exist, must be provided. Where the information provided does not fully identify a formulant, an appropriate specification must be provided. The trade name of formulants, where they exist, must also be provided.

1.4.4 For formulants their function must be given:

adhesive (sticker)	dye	repellent
antifoaming agent	emetic	safener
antifreeze	emulsifier	solvent
binder	fertilizer	stabiliser
buffer	preservative	synergist
carrier	odorant	thickener
deodorant	perfume	wetting agent
dispersing agent	propellant	miscellaneous (specify)

1.5 ***Physical state and nature of the preparation (emulsifiable concentrate, wettable powder, solution etc.)***

1.5.1 The type and code of the preparation must be designated in accordance with the "Catalogue of pesticide formulation types and international coding system (GIFAP Technical Monograph No 2 1989)".

Where a particular preparation is not defined precisely in that publication, a full description of the physical nature and state of the preparation must be provided, together with a proposal for a suitable description of the type of preparation and a proposal for its definition.

1.6 ***Function (herbicide, insecticide, etc.)***

The function must be specified from among the following:

acaricide	molluscicide	semio-chemicals

bactericide	nematicide	talpicide
fungicide	plant growth regulator	viricide
herbicide	repellent	other (must be specified)
insecticide	rodenticide	

2 Physical, chemical and technical properties of the plant protection product

The extent to which plant protection products for which authorization is sought, comply with relevant FAO specifications as agreed by the Group of Experts on Pesticide Specifications, of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements and Application Standards, must be stated. Divergences from FAO specifications must be described in detail, and justified.

2.1 *Appearance (colour and odour)*

A description of both the colour and odour, if any, and the physical state of the preparation, must be provided.

2.2 *Explosivity and oxidizing properties*

2.2.1 The explosive properties of preparations must be determined in accordance with EEC Method A 14 and be reported. Where available thermodynamic information establishes beyond reasonable doubt, that the preparation is incapable of exothermic reaction, it is sufficient to provide that information as a justification for not determining the explosive properties of the preparation.

2.2.2 The oxidizing properties of preparations that are solids, must be determined in accordance with EEC Method A 17 and be reported. For other preparations the method used must be justified. Oxidizing properties do not have to be determined if it can be shown without reasonable doubt, on the basis of thermodynamic information, that the preparation is incapable of reacting exothermically with combustible materials.

2.3 *Flash point and other indications of flammability or spontaneous ignition*

The flash point of liquids that contain flammable solvents, must be determined in accordance with EEC Method A 9 and be reported. The flammability of solid preparations and gasses must be determined in accordance with EEC Method A 10, A 11 or A 12, as appropriate, and be reported. The auto-flammability of preparations, determined in accordance with EEC Method A 15 or A 16 as appropriate, and/or, where necessary, in accordance with the UN-Bowes-Cameron-Cage-Test (UN-Recommendations on the Transport of Dangerous Goods, Chapter 14, Nr.14.3.4), must be reported.

2.4 *Acidity/alkalinity and if necessary pH value*

2.4.1 In the case of preparations that are acidic (pH < 4) or alkaline (pH > 10) the acidity or alkalinity and the pH value must be determined in accordance with CIPAC Method MT 31 and MT 75 respectively, and be reported.

2.4.2 Where relevant (if to be applied as aqueous dilution) the pH of a 1 % aqueous dilution, emulsion or dispersion of the preparation, must be determined in accordance with CIPAC Method MT 75 and be reported.

2.5 ***Viscosity and surface tension***

2.5.1 In the case of liquid preparations for Ultra Low Volume use (ULV) kinematic viscosity must be determined in accordance with OECD Test Guideline 14 and be reported.

2.5.2 For non newtonian liquids viscosity must be determined and reported together with the test conditions.

2.5.3 In the case of liquid preparations surface tension must be determined in accordance with EEC Method A 5 and be reported.

2.6 ***Relative density and bulk density***

2.6.1 The relative density of liquid preparations must be determined in accordance with EEC Method A 3 and be reported.

2.6.2 The bulk (tap) density of preparations that are powders or granules, must be determined in accordance with CIPAC Methods MT 33, MT 159 or MT 169, as appropriate, and be reported.

2.7 ***Storage stability - stability and shelf-life. Effects of light, temperature and humidity on technical characteristics of the plant protection product***

2.7.1 The stability of the preparation after storage for 14 days at 54 °C must be determined in accordance with CIPAC Method MT 46 and be reported.

Other storage times and/or temperatures may be needed (*e.g.* 8 weeks at 40 °C or 12 weeks at 35 °C or 18 weeks at 30 °C) if the preparation is heat sensitive.

If the active substance content after the heat stability test has decreased by more than 5 % of the initial determined content, the minimum content must be declared and information on the degradation products must be supplied.

2.7.2 Additionally in the case of liquid preparations, the effect of low temperatures on stability, must be determined in accordance with CIPAC Methods MT 39, MT 48, MT 51 or MT 54, as appropriate, and be reported.

2.7.3 The shelf life of the preparation at ambient temperatures must be reported. Where shelf life is less than two years, the shelf life in months, with appropriate temperature specifications, must be reported. GIFAP Monograph No 17 contains useful information on such testing..

2.8 ***Technical characteristics of the plant protection product***

The technical characteristics of the preparation must be determined to permit a decision to be made as to its acceptability.

2.8.1 *Wettability*

The wettability of solid preparations that are diluted for use (*e.g.* wettable powders, water soluble powders, water soluble granules and water dispersible granules) must be determined in accordance with CIPAC Method MT 53.3 and be reported.

2.8.2 *Persistent foaming*

The persistence of foaming of preparations to be diluted with water, must be determined in accordance with CIPAC Method MT 47 and be reported.

2.8.3 *Suspensibility and suspension stability*

2.8.3.1 The suspensibility of water dispersible products (*e.g.* wettable powders, water dispersible granules, suspension concentrates) must be determined in accordance with CIPAC Method MT 15, MT 161 or MT 168, as appropriate and be reported.

2.8.3.2 The spontaneity or dispersibility of water dispersible products (*e.g.* suspension concentrates and water dispersible granules) must be determined in accordance with CIPAC Methods MT 160 or MT 174, as appropriate, and be reported.

2.8.4 *Dilution stability*

The dilution stability of water soluble products must be determined in accordance with CIPAC Method MT 41 and be reported.

2.8.5 *Dry sieve test and wet sieve test*

In order to ensure that dustable powders have a suitable particle size distribution for ease of application, a dry sieve test must be conducted in accordance with CIPAC Method MT 59.1, and be reported.

In the case of water dispersible products, a wet sieve test must be conducted in accordance with CIPAC Method MT 59.3 or MT 167, as appropriate, and be reported.

2.8.6 *Particle size distribution (dustable and wettable powders, granules), content of dust/fines (granules), attrition and friability (granules)*

2.8.6.1 The size distribution of particles in the case of powders, must be determined in accordance with OECD Method 110 and be reported.

The nominal size range of granules for direct application must be determined in accordance with CIPAC MT 58.3 and for water dispersible granules and in accordance with CIPAC MT 170, and be reported.

2.8.6.2 The dust content of granular preparations, must be determined in accordance with CIPAC Method MT 171 and be reported. If relevant for operator exposure the particle size of dust must be determined in accordance with OECD Method 110 and be reported.

2.8.6.3 The friability and attrition characteristics of granules, must be determined and reported once internationally agreed methods are available. Where relevant data are available they must be reported together with details of the method used.

2.8.7 *Emulsifiability, Re-emulsifiability, emulsion stability*

2.8.7.1 The emulsifiability, emulsion stability and re-emulsifiability of preparations that form emulsions, must be determined in accordance with CIPAC Methods MT 36 or MT 173, as appropriate, and be reported.

2.8.7.2 The stability of dilute emulsions and of preparations that are emulsions, must be determined in accordance with CIPAC Method MT 20 or MT 173, as appropriate, and be reported.

2.8.8 *Flowability, pourability (rinsability) and dustability*

2.8.8.1 The flowability of granular preparations must be determined in accordance with CIPAC Method MT 172 and be reported.

2.8.8.2 The pourability (including rinsed residue) of suspensions (*e.g.* suspension concentrates, suspo-emulsions), must be determined in accordance with CIPAC Method MT 148 and be reported.

2.8.8.3 The dustability of dustable powders following accelerated storage as specified in paragraph 2.7.1 must be determined in accordance with CIPAC Method MT 34 or another suitable method and be reported.

2.9 ***Physical and chemical compatibility with other products including plant protection products with which its use is to be authorized***

2.9.1 The physical compatibility of tank mixes must be determined using in-house test methods and be reported. A practical test is an acceptable alternative.

2.9.2 The chemical compatibility of tank mixes must be determined and be reported except where examination of the individual properties of the preparations establishes beyond reasonable doubt that there is no possibility of reaction taking place. In such cases it is sufficient to provide that information as justification for not determining chemical compatibility.

2.10 ***Adherence and distribution to seeds***

In the case of preparations for seed treatment, both distribution and adhesion must be investigated and be reported; in the case of distribution in accordance with CIPAC Method MT 175.

2.11 ***Summary and evaluation of data presented under points 2.1 to 2.10***

3 **Data on application**

3.1 ***Field of use envisaged, e.g. field, protected crops, storage of plant products, home gardening***

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

Field use
- Agriculture
- Horticulture
- Forestry
- Viticulture

Protected crops

Amenity

Weed control on non-cultivated areas

Home gardening

House plants

Plant products storage practice

Other (specify)

3.2 ***Effects on harmful organisms, e.g. contact, inhalation or stomach poison, fungitoxic or fungistatic, etc., systemic or not in plants***

3.2.1 The nature of the effects on harmful organisms must be stated:

contact action	fungitoxic action	reproduction inhibitor
stomach action	fungistatic action	other (must be specified)
inhalation action	desiccant	

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

3.3 ***Details of intended use e.g. types of harmful organisms controlled and/or plants or plant products to be protected***

Details of the intended use must be provided.

Where relevant, effects achieved *e.g.* sprout suppression, retardation of ripening, reduction in stem length, enhanced fertilization *etc.* must be reported.

3.4 ***Application rate***

For each method of application and each use, the rate of application per unit (ha, m^2, m^3) treated, in terms of g or kg of both preparation and active substance, must be provided.

Application rates must normally be expressed in g or kg/ha or in kg/m^3 and where appropriate in g or kg/tonne; for protected crops and home gardening use, rates must be expressed in g or kg/100 m^2 or g or kg/m^3.

3.5 ***Concentration of active substance in material used (e.g. in the diluted spray, baits or treated seed)***

The content of active substance must be reported, as appropriate, in g/l, g/kg, mg/kg or in g/tonne.

3.6 ***Method of application***

The method of application proposed must be described fully, indicating the type of equipment to be used, if any, as well as the type and volume of diluent to be used per unit of area or volume.

3.7 ***Number and timing of applications and duration of protection***

The maximum number of applications to be used and their timing, must be reported. Where relevant the growth stages of the crop or plants to be protected and the development stages of the harmful organisms, must be indicated. Where possible the interval between applications, in days, must be stated.

The duration of protection afforded both by each application and by the maximum number of applications to be used, must be indicated.

3.8 ***Necessary waiting periods or other precautions to avoid Phytotoxic effects on succeeding crops***

Where relevant, minimum waiting periods between last application and sowing or planting of succeeding crops, that are necessary to avoid phytotoxic effects on succeeding crops, must be stated, and follow from the data provided in accordance with point 6.6.

Limitations on choice of succeeding crops, if any, must be stated.

3.9 ***Proposed instructions for use***

The proposed instructions for use of the preparation, to be printed on labels and leaflets, must be provided.

4 Further information on the plant protection product

4.1 *Packaging (type, materials, size etc.), compatibility of the preparation with proposed packaging materials*

4.1.1 Packaging to be used must be fully described and specified in terms of the materials used, manner of construction (*e.g.* extruded, welded *etc.*), size and capacity, size of opening, type of closure and seals. It must be designed in accordance with the criteria and guidelines specified in the FAO "Guidelines for the Packaging of Pesticides".

4.1.2 The suitability of the packaging, including closures, in terms of its strength, leakproofness and resistance to normal transport and handling, must be determined in accordance with ADR Methods 3552, 3553, 3560, 3554, 3555, 3556 and 3558, or ADR methods for intermediate bulk containers, as appropriate, and where child resistant closures are required, in accordance with ISO Standard 8317, and be reported.

4.1.3 The resistance of the packaging material to its contents must be determined in accordance with GIFAP Monograph no. 17, and be reported.

4.2 *Procedures for cleaning application equipment*

Cleaning procedures for both application equipment and protective clothing must be described in detail. The effectiveness of the cleaning procedure, must be fully investigated and reported.

4.3 *Re-entry periods, necessary waiting periods or other precautions to protect man, livestock and the environment*

The information provided must follow from and be supported by the data provided for the active substance(s) and that provided under Sections 7 and 8.

4.3.1 Where relevant, pre-harvest intervals, re-entry periods or withholding periods necessary to minimize the presence of residues in or on crops, plants and plant products, or in or on treated areas or spaces, with a view to protecting man or livestock, must be specified *e.g.*

- pre-harvest interval (in days) for each relevant crop;
- re-entry period (in days) for livestock, to areas to be grazed;
- re-entry period (in hours or days) for man to crops, buildings or spaces treated;
- withholding period (in days) for animal feedingstuffs;
- waiting period (in days), between application and handling treated products; or
- waiting period (in days), between last application and sowing or planting succeeding crops.

4.3.2 Where necessary, in the light of test results, information on any specific agricultural, plant health or environmental conditions under which the preparation may or may not be used, must be provided.

4.4 *Recommended methods and precautions concerning: handling, storage, transport or fire*

The recommended methods and precautions concerning handling procedures (detailed) for the storage, at both warehouse and user level of plant protection products, for their transport and in the event of fire must be provided. Where available, information on combustion products must be provided. The risks likely to arise and the methods and procedures to minimize the hazards arising, must be specified. Procedures to preclude or minimize the generation of waste or leftovers must be provided.

Where relevant, assessment must be conducted in accordance with ISO-TR 9122.

Where relevant, the nature and characteristics of protective clothing and equipment proposed must be reported. The data provided must be sufficient to permit an evaluation to be made of the suitability and effectiveness of the protective clothing and equipment concerned under realistic conditions of use (*e.g.* field or glasshouse circumstances).

4.5 ***Emergency measures in the case of an accident***

Whether arising during transport, storage or use, detailed procedures to be followed in the event of an emergency, must be provided, and include procedures for -

- containment of spillages,
- decontamination of areas, vehicles and buildings,
- disposal of damaged packaging, adsorbents and other materials,
- protection of emergency workers and bystanders, and
- first aid measures.

4.6 ***Procedures for destruction or decontamination of the plant protection product and its packaging***

Procedures for destruction and decontamination must be developed for both small quantities (user level) and large quantities (warehouse level). The procedures must be consistent with provisions in place relating to the disposal of waste and of toxic waste. The means of disposal proposed should be without unacceptable influence on the environment and be the most cost effective and practical means of disposal feasible.

4.6.1 *Possibility of neutralization*

Neutralization procedures (*e.g.* by reaction with alkali to form less toxic compounds) for use in the event of accidental spillages, must where they are feasible, be described. The products produced after neutralization should be identified (through analysis or on the basis of theoretical considerations)and be reported.

4.6.2 *Controlled incineration*

In many cases the preferred or sole means to safely dispose of active substances as well as plant protection products containing them, contaminated materials, or contaminated packaging, is through controlled incineration in a licensed incinerator.

Where the content of halogens of the active substance(s) in the preparation is greater than 60 %, the pyrolytic behaviour of the active substance under controlled conditions (including, where relevant, supply of oxygen and residence time), at 800 °C and the content of polyhalogenated dibenzo-p-dioxins and dibenzo-furans in the products of pyrolysis must be reported. The applicant must provide detailed instructions for safe disposal.

4.6.3 *Others*

Other methods to dispose of plant protection products, packaging and contaminated materials, where proposed, must be fully described. Data must be provided for such methods, to establish their effectiveness and safety.

5 **Analytical methods**

Introduction

The provisions of this section only cover analytical methods for post-registration control and monitoring purposes.

For analytical methods used for the generation of data as required in accordance with Annex IIIA, or for other purposes, applicants must provide a justification for the method used-, where necessary separate guidance will be developed for such methods on the basis of the same requirements defined for methods for post-registration control and monitoring purposes.

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

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

For the purposes of point 5 of this Annex, the following definitions apply:

impurities	any component other than the pure active substance that is present in the active substance as manufactured (including non- active isomers) originating from the manufacturing process or from degradation during storage;
relevant impurities	impurities of toxicological and/or ecotoxicological or environmental concern;
metabolites	metabolites include products resulting from degradation or reaction of the active substance;
relevant metabolites	metabolites of toxicological and/or ecotoxicological or environmental concern.

On request the following samples must be provided:

- samples of the preparation,
- analytical standards of the pure active substance,
- samples of the active substance as manufactured,
- analytical standards of relevant metabolites and all other components included in the residue definition,
- if available, samples of reference substances for relevant impurities.

For definitions see Annex IIA, points 4.1 and 4.2.

5.1 ***Methods for the analysis of the preparation***

5.1.1 Methods, which must be described in full, must be provided for the determination of the active substance in the preparation. In the case of a preparation containing more than one active substance a method capable of determining each, in the presence of the other, should be provided. If a combined method is not submitted, the technical reasons must be stated. The applicability of existing CIPAC methods must be reported.

5.1.2 Methods must also be provided for the determination in the preparation of relevant impurities, if the composition of the preparation is such that - on the basis of theoretical consideration - such impurities may be formed during manufacture or result from degradation during storage.

If required methods for the determination of formulants or constituents of formulants in the preparation must be submitted.

5.1.3 *Specificity, linearity, accuracy and repeatability*

5.1.3.1 Specificity of methods submitted must be demonstrated and be reported. In addition the extent of interference by other substances present in the preparation must be determined.

While interferences due to other components may be identified as systematic errors, in the assessment of the accuracy of methods proposed, an explanation must be provided for any interference occurring which contributes more than ± 3 % to the total quantity determined.

5.1.3.2 The linearity of proposed methods over an appropriate range must be determined and be reported. The calibration range must extend (by at least 20 %) the highest and lowest nominal content of the analyte in relevant analytical solutions of the preparation. Duplicative calibration determinations must be made at 3 or more concentrations. Alternatively, 5 concentrations, each as single measurements, are acceptable. Reports submitted must include the equation of the calibration line and the correlation co-efficient and representative and properly labelled documentation from the analysis, *e.g.* chromatograms.

5.1.3.3 Accuracy is normally only required for methods for the determination of pure active substance and relevant impurities in the preparation.

5.1.3.4 For the determination of repeatability, a minimum of five determinations must in principle be made. Relative standard deviation (% RSD) must be reported. Outliers identified through an appropriate method (*e.g.* Dixon's or Grubb's Test), may be discarded. Where outliers have been discarded, that fact must be clearly indicated. An explanation as to the reason for the occurrence of individual outliers must be attempted.

5.2 ***Analytical methods for the determination of residues***

Analytical methods for the determination of residues must be submitted unless it is justified that the methods already submitted according to the requirements of Annex IIA, point 4.2 can be applied.

The same provisions as provided in Annex IIA, point 4.2, apply.

6 Efficacy data

General

The data supplied must be sufficient to permit an evaluation of the plant protection product to be made. In particular it must be possible to evaluate the nature and extent of benefits that accrue following use of the preparation, where they exist in comparison to suitable reference products and damage thresholds, and to define its conditions of use.

The number of trials to be conducted and reported depends mainly on factors such as the extent to which the properties of the active substance(s) it contains are known and on the range of conditions that arise, including variability in plant health conditions, climatic differences, the range of agricultural practices, the uniformity of the crops, the mode of application, the type of harmful organism and the type of plant protection product.

Sufficient data must be generated and submitted to confirm that patterns determined hold for the regions and the range of conditions, likely to be encountered in the regions concerned, for which its use is to be recommended. Where an applicant claims that tests in one or more of the proposed regions of use are unnecessary because conditions are comparable with those in other regions where tests have been carried out, the applicant must substantiate the claim for comparability with documentary evidence.

In order to assess seasonal differences, if any, sufficient data must be generated and submitted to confirm the performance of the plant protection products in each agronomically and climatically different region for each particular crop (or commodity)/ harmful organism combination. Normally trials on effectiveness or phytotoxicity, where relevant, in at least two growing seasons must be reported.

If in the opinion of the applicant the trials from the first season adequately confirm the validity of claims made on the basis of extrapolation of results from other crops, commodities or situations or from tests with closely similar preparations, a justification, which is acceptable to the competent authority for not carrying out a second season's work must be provided. Conversely, where, because of climatic or plant health conditions or other reasons, the data obtained in any particular season are of limited value for the assessment of performance, trials in one or more further seasons must be conducted and reported.

6.1 *Preliminary tests*

Reports in summary form of preliminary tests, including glasshouse and field studies, used to assess the biological activity and dose range finding of the plant protection product and of the active substance(s) it contains, must be submitted when requested by the competent authority. These reports will provide additional information for the competent authority when it evaluates the plant protection product. Where this information is not submitted a justification that is acceptable to the competent authority must be provided.

6.2 ***Testing effectiveness***

Aim of the tests

The tests shall provide sufficient data to permit an evaluation of the level, duration and consistency of control or protection or other intended effects of the plant protection product in comparison to suitable reference products, where they exist.

Test conditions

Normally a trial consists of three components: test product, reference product and untreated control.

The performance of the plant protection product must be investigated in relation to suitable reference products, where they exist. A suitable reference product is defined as an authorized plant protection product that has proved to have a sufficient performance in practice under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use. In general, formulation type, effects on the harmful organisms, working spectrum and method of application should be close to those of the tested plant protection product.

Plant protection products must be tested in circumstances where the target harmful organism has been shown to have been present at a level causing or known to cause adverse effects (yield, quality, operational benefit) on an unprotected crop or area or on plants or plant products which have not been treated or where the harmful organism is present at such a level that an evaluation of the plant protection product can be made.

Trials to provide data on plant protection products for control of harmful organisms must show the level of control of the species of harmful organisms concerned or of species representative of groups for which claims are made. Trials must include the different stages of growth or life cycle of the harmful species, where this is relevant and the different strains or races, where these are likely to show different degrees of susceptibility.

Similarly, trials to provide data on plant protection products which are plant growth regulators, must show the level of effects on the species to be treated, and include investigation of differences in the response of a representative sample of the range of cultivars on which its use is proposed.

In order to clarify the dose response, dose rates lower than the recommended one must be included in some trials in order to enable to assess whether the recommended rate is the minimum necessary to achieve the desired effect.

The duration of the effects of treatment must be investigated in relation to the control of the target organism or effect on the treated plants or plant products, as appropriate. When more than one application is recommended, trials must be reported which establish the duration of the effects of an application, the number of applications necessary and the desired intervals between them.

Evidence must be submitted to show that the dose, timing and method of application recommended give adequate control, protection or have the intended effect in the range of circumstances likely to be encountered in practical use.

Unless there are clear indications that the performance of the plant protection product is unlikely to be affected to a significant degree by environmental factors, such as temperature or

rain, an investigation of the effects of such factors on performance must be carried out and reported, particularly where it is known that the performance of chemically related products is so affected.

Where proposed label claims include recommendations for the use of the plant protection product with other plant protection product(s) or adjuvant(s) information on the performance of the mixture must be provided.

Test guideline

Trials must be designed to investigate specified issues, to minimize the effects of random variation between different parts of each site and to enable statistical analysis to be applied to results amenable to such analysis. The design, analysis and reporting of trials must be in accordance with European and Mediterranean Plant Protection Organisation (EPPO) guidelines 152 and 181. The report shall include a detailed and critical assessment of the data.

When conducted within the territory of the State, the trials must be carried out in accordance with specific EPPO guidelines, where available. When conducted within the territory of another Member State, the trials must be carried out in accordance with specific EPPO guidelines, where available or when the Member State concerned so requires, in accordance with guidelines satisfying at least the requirements of the corresponding EPPO guidelines.

A statistical analysis of results amenable to such analysis must be carried out; where necessary the test guideline used must be adapted to enable such analysis.

6.3 ***Information on the occurrence or possible occurrence of the development of resistance***

Laboratory data and where it exists, field information relating to the occurrence and development of resistance or cross-resistance in populations of harmful organisms to the active substance(s), or to related active substances, must be provided. Where such information is not directly relevant to the uses for which authorization is sought or to be renewed (different species of harmful organism or different crops), it must, if available, nevertheless be provided, as it may provide an indication of the likelihood of resistance developing in the target population.

Where there is evidence or information to suggest that, in commercial use, the development of resistance is likely, evidence must be generated and submitted as to the sensitivity of the population of the harmful organism concerned to the plant protection product. In such cases a management strategy designed to minimize the likelihood of resistance of cross-resistance developing in target species must be provided.

6.4 ***Effects on the yield of treated plants or plant products in terms of quantity and/or quality***

6.4.1 *Effects on the quality of plants or plant products*

Aim of the tests

The tests shall provide sufficient data to permit an evaluation of the possible occurrence of taint or odour or other quality aspects of plants or plant products after treatment with the plant protection product.

Circumstances in which required

The possibility of the occurrence of taint or odour in food crops must be investigated and be reported where -

- the nature of the product or its use is such that a risk of occurrence of taint or odour might be expected, or
- other products based on the same or a closely similar active substance have been shown to present a risk of occurrence of taint or odour.

The effects of plant protection products on other quality aspects of treated plants or plant products must be investigated and reported where -

- the nature of the plant protection product or its use could have an adverse influence on other quality aspects (for example in the case of use of plant growth regulators close to harvest), or
- other products based on the same or closely similar active substances have been shown to have an adverse influence on the quality.

Testing should be conducted initially on the main crops on which the plant protection product is to be used, at twice the normal rates of application and using, where relevant, the main methods of processing. Where effects are observed it is necessary to perform testing at the normal rate of application.

The extent of investigation necessary on other crops will depend on their degree of similarity to the main crops already tested, the quantity and quality of data available on those main crops and how far the manner of use of the plant protection product and methods of processing the crops, if relevant, are similar. It is generally sufficient to perform the test with the main formulation type to be authorized.

6.4.2 *Effects on transformation processes*

Aim of the tests

The tests shall provide sufficient data to permit an evaluation of the possible occurrence of adverse effects after treatment with the plant protection product on transformation processes or on the quality of their products.

Circumstances in which required

When the treated plants or plant products are normally intended for use in transformation process such as wine making, brewing or bread making and when at harvest significant residues are present, the possibility of the occurrence of adverse effects must be investigated and reported where -

- there are indications that the use of the plant protection product could have an influence on the processes involved (for example in the case of use of plant growth regulators or fungicides close to harvest), or
- other products based on the same or closely similar active substances have been shown to have an adverse influence on these processes or its products.

It is generally sufficient to perform the test with the main formulation type to be authorized.

6.4.3 *Effects on the yield of treated plants or plant products*

Aim of the tests

The tests shall provide sufficient data to permit an evaluation of the performance of the plant protection product and of the possible occurrence of yield reduction or loss in storage of treated plants or plant products.

Circumstances in which required

The effects of plant protection products on the yield or yield components of treated plants or plant products must be determined where relevant. When treated plants or plant products are likely to be stored the effect on the yield after storage, including data on storage life must be determined where relevant.

This information will normally be available from the tests required under the provisions of point 6.2.

6.5 ***Phytotoxicity to target plants (including different cultivars), or to target plant products***

Aim of the tests

The tests shall provide sufficient data to permit an evaluation of the performance of the plant protection product and of the possible occurrence of phytotoxicity after treatment with the plant protection product.

Circumstances in which required

For herbicides and for other plant protection products for which adverse effects, however transitory, are seen during the trials, performed in accordance to point 6.2, the margins of selectivity on target crops must be established, using twice the recommended rate of application. Where serious phytotoxic effects are seen, an intermediate application rate must also be investigated.

Where adverse effects occur, but are claimed to be unimportant in comparison with the benefits of use or to be transient, evidence to support this claim is required. If necessary yield measurements must be submitted.

The safety of a plant protection product to the main cultivars of the main crops for which it is recommended must be demonstrated, including effects of crop growth stage, vigour, and other factors which may influence susceptibility to damage or injury.

The extent of investigation necessary on other crops will depend on their degree of similarity to the main crops already tested, the quantity and quality of data available on those main crops and how far the manner of use of the plant protection product, if relevant, is similar. It is generally sufficient to perform the test with the main formulation type to be authorized.

Where proposed label claims include recommendations for the use of the plant protection product with other plant protection product(s) or adjuvant(s), the provision of the previous paragraphs apply for the mixture.

Test guideline

Observations concerning phytotoxicity must be recorded and reported in the tests provided for under point 6.2.

Where phytotoxic effects are seen, they must be accurately assessed and recorded in accordance with EPPO Guideline 135, where testing is conducted within the territory of the State. When conducted within the territory of another Member State, the trials must be carried out in accordance with EPPO Guideline 135, or when the Member State concerned so requires, in accordance with guidelines satisfying at least the requirements of EPPO Guideline 135.

A statistical analysis of results amenable to such analysis must be carried out, where necessary the test guideline used must be adapted to enable such analysis.

6.6 ***Observations on undesirable or unintended side-effects e.g. on beneficial and other non-target organisms, on succeeding crops, other plants or parts of treated plants used for propagating purposes (e.g. seeds, cuttings, runners)***

6.6.1 *Impact on succeeding crops*

Aim of the information required

Sufficient data must be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on succeeding crops.

Circumstances in which required

Where data, generated in accordance with section 9, point 9.1, shows that significant residues of the active substance, its metabolites or degradation products, which have or may have biological activity on succeeding crops, remain in soil or in plant materials, such as straw or organic material up to sowing or planting time of possible succeeding crops, observations must be submitted on effects on the normal range of succeeding crops.

6.6.2 *Impact on other plants, including adjacent crops*

Aim of the information required

Sufficient data must be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on other plants, including adjacent crops.

Circumstances in which required

Observations must be submitted on adverse effects on other plants, including the normal range of adjacent crops, when there are indications that the plant protection product could affect these plants *via* vapour drift.

6.6.3 *Impact on treated plants or plant products to be used for propagation*

Aim of the information required

Sufficient data must be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on plants or plant products to be used for propagation.

Circumstances in which required

Observations must be submitted on the impact of plant protection products on plant parts used for propagation except where the proposed uses preclude use on crops intended for production of seeds, cuttings, runners or tubers for planting, as appropriate:

(i) For seeds - viability, germination and vigour

(ii) Cuttings - rooting and growth rates

(iii) Runners - establishment and growth rates

(iv) Tubers - sprouting and normal growth

Test guideline

For seeds testing shall be done according to ISTA methods [61].

6.6.4 *Effects on beneficial and other non-target organisms*

Any effects, positive or negative, on the incidence of other harmful organisms, observed in the tests performed in accordance with the requirements of this section, shall be reported. Any observed environmental effects must also be reported, especially effects on wildlife and/or beneficial organisms.

6.7 ***Summary and evaluation of data presented under points 6.1 to 6.6***

A summary of all data and information provided under points 6.1 to 6.6 must be provided, together with a detailed and a critical assessment of the data, with particular reference to the benefits that the plant protection product offers, adverse effects that do or may arise and measures necessary to avoid or minimize adverse effects.

[61] International Rules for Seed Testing, 1985. Proceedings of the International Seed Testing Association, Seed Science and Technology, Volume 13, Number 2, 1985

7 Toxicological studies

For the evaluation of the toxicity of preparations, sufficient information concerning the acute toxicity, irritancy and sensitising properties of their active substance(s) is necessary. Where possible, additional information on mode of toxic action, toxicological profile and all other known toxicological aspects of the active substance(s) should be submitted.

In the context of the influence that impurities and other components can have on toxicological behaviour, it is essential that for each study submitted, a detailed description (specification) of the material used, be provided. Tests must be conducted using the plant protection to be authorized.

7.1 *Acute toxicity*

The studies, data and information to be provided and evaluated must be sufficient to permit the identification of effects following a single exposure to the plant protection product, and in particular to establish or indicate -

- the toxicity of the plant protection product,
- the toxicity of the plant protection product relative to that of the active substance,
- the time course and characteristics of the effects with full details of behavioural changes and possible gross pathological changes at post-mortem,
- where possible mode of toxic action, and
- the relative hazard associated with the different routes of exposure.

While the emphasis must be on estimating the toxicity ranges involved, the information generated must also permit the plant protection product to be classified in accordance with the Regulations of 2001. The information generated through acute toxicity testing is of particular value in assessing hazards likely to arise in accident situations.

7.1.1 *Oral*

Circumstances in which required

An acute oral toxicity test should always be carried out unless the applicant can establish to the satisfaction of the competent authority that Regulation 9 (1) (a) of the Regulations of 2001 can be invoked.

Test Guideline

The test must be carried out in accordance with EEC Method B 1 or B 1 bis.

7.1.2 *Percutaneous*

Circumstances in which required

An acute percutaneous toxicity test should always be carried out unless the applicant can establish to the satisfaction of the competent authority that Regulation 9 (1) (a) of the Regulations of 2001 can be invoked.

Test Guideline

The test must be carried out in accordance with EEC Method B 3.

7.1.3 *Inhalation*

Aim of the test

The test will provide information concerning the inhalation toxicity to rats of the plant protection product or of smoke generated from it.

Circumstances in which required

The test must be carried out where the plant protection product -

- is a gas or a liquefied gas,
- is a smoke generating formulation or a fumigant,
- is used with fogging equipment,
- is a vapour releasing preparation,
- is an aerosol,
- is a powder containing a significant proportion of particles of diameter < 50 μm (> 1 % on a weight basis),
- is to be applied from aircraft in cases where inhalation exposure is relevant,
- contains an active substance with a vapour pressure > 1 x 10^{-2} Pa and is to be used in enclosed spaces such as warehouses or glasshouses,
- is to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 μm (> 1 % on a weight basis).

Test Guideline

The test must be carried out in accordance with EEC Method B 2.

7.1.4 *Skin irritation*

Aim of the test

The test will provide information as to the potential for skin irritancy of the plant protection product, including the potential reversibility of the effects observed.

Circumstances in which required

The skin irritancy of the plant protection product must be determined and reported except where it is likely, as indicated in the test guideline, that severe skin effects may be produced or that effects can be excluded.

Test Guideline

The test must be carried out in accordance with EEC Method B 4.

7.1.5 *Eye irritation*

Aim of the test

The test will provide information as to the potential for eye irritancy of the plant protection product, including the potential reversibility of the effects observed.

Circumstances in which required

Eye irritation tests must be conducted and reported except where it is likely, as indicated in the test guideline, that severe effects on the eye may be produced.

Test Guideline

The test must be carried out in accordance with EEC Method B 5.

7.1.6 *Skin sensitisation*

Aim of the test

The test will provide sufficient information to assess the potential of the plant protection product to provoke skin sensitisation reactions.

Circumstances in which required

The test must always be carried out except where the active substance(s) or co-formulants are known to have sensitising properties.

Test Guideline

The test must be carried out in accordance with EEC Method B 6.

7.1.7 *Supplementary studies for combinations of plant protection products*

Aim of the test

In certain cases it may be necessary to carry out the tests as referred to in points 7.1.1 to 7.1.6 for a combination of plant protection products where the product label includes requirements for use of the plant protection product with other plant protection products and/or with adjuvants, as a tank mix. Decisions as to the need for supplementary studies must be made on a case by case basis, taking into account the results of the acute toxicity studies of the individual plant protection products, the possibility for exposure to the combination of the products concerned and available information or practical experience with the products concerned or similar products.

7.2 ***Data on exposure***

7.2.1 *Operator exposure*

The risks for those using plant protection products depend on the physical, chemical and toxicological properties of the plant protection product as well as the form of the product (undiluted/diluted), and the route, degree and duration of exposure. Sufficient information and data must be generated and reported to permit an assessment to be made of the extent of exposure to the active substance(s) and/or toxicologically relevant compounds in the plant protection product likely to occur under the proposed conditions for its use. The data and information provided must also provide a basis for the selection of the appropriate protective measures including personal protective equipment to be used by operators and to be specified on the label.

7.2.1.1 *Estimation of operator exposure*

Aim of the estimation

An estimation shall be made, using where available a suitable calculation model, in order to permit an evaluation to be made of the degree of operator exposure likely to arise under the proposed conditions of use.

Circumstances in which required

An estimation of operator exposure must always be completed.

Estimation conditions

An estimation shall be made for each type of application method and application equipment proposed for use of the plant protection product, taking account of the requirements arising from the application of the classification and labelling provisions of the Directive of 1978. The estimation made shall relate to exposure arising from handling the undiluted and diluted product, taking into account the different types and sizes of containers to be used, mixing and loading operations, application of the plant protection product, climatic conditions and cleaning and the routine maintenance of application equipment.

A first estimation shall be made on the basis of the assumption that the operator does not use any personal protective equipment.

Where appropriate, a second estimation shall be made on the basis of an assumption that the operator uses that effective and readily obtainable protective equipment which it is feasible for the operator to use. Where personal protective measures are specified on the label, the estimation shall take these into account.

7.2.1.2 *Measurement of operator exposure*

Aim of the test

The test shall provide sufficient data to permit an evaluation to be made of the degree of operator exposure likely to arise under the proposed conditions of use.

Circumstances in which required

Actual exposure data for relevant exposure route(s) must be reported where risk assessment indicates that a health-based limit value may be exceeded. That will be the case when the results of the estimation of operator exposure provided for under point 7.2.1.1 indicate that -

- the Acceptable Operator Exposure Level(s) (AOEL) established in the context of the inclusion of the active substance(s) in Annex I, and/or
- the Limit Values established for the active substance(s) and/or toxicologically relevant compound(s) contained in the plant protection product, in accordance with Council Directive 80/1107/EEC and Council Directive 90/394/EEC [62], on the protection of workers from the risks related to exposure to carcinogens at work,

may be exceeded.

Actual exposure data must also be reported when an appropriate calculation model or appropriate data are not available to permit an estimation to be made as provided for in point 7.2.1.1.

In cases where dermal exposure is the most important exposure route, a dermal absorption test or the results of a sub-acute dermal study, if not already available, may be a useful alternative test, to provide data to be used in refining the estimation made in accordance with point 7.2.1.1.

Test conditions

[62] O.J. No. L196/1 26/7/1990

The test must be conducted under realistic exposure conditions taking into account the proposed conditions of use.

When measuring exposure to a plant protection product in the air within the breathing space of operators, the requirements for measuring procedures described in Annex IIA to Council Directive 80/1107/EEC of 27 November 1980 on the protection of workers from the risks related to exposure to chemical, physical and biological agents at work must be taken into account

7.2.2 *Bystander exposure*

Bystanders can be exposed during the application of plant protection products. Sufficient information and data must be reported to provide a basis for the selection of appropriate conditions of use for the protection of bystanders, including the exclusion of bystanders from treatment areas and separation distances.

Aim of the estimation

An estimation shall be made, using where available a suitable calculation model, in order to permit an evaluation to be made of the degree of bystander exposure likely to arise under the proposed conditions of use.

Circumstances in which required

An estimation of bystander exposure must always be completed.

Estimation conditions

An estimation of bystander exposure shall be made for each type of application method. The estimation shall be made on the basis of the assumption that bystanders do not use any personal protective equipment.

Measurement of bystander exposure may be required when estimates made indicate that there is cause for concern.

When measuring exposure to a plant protection product in the air within the breathing space of bystanders, the requirements for measuring procedures described in Annex IIA to Council Directive 80/1107/EEC of 27 November 1980 on the protection of workers from the risks related to exposure to chemical, physical and biological agents at work must be taken into account

7.2.3 *Worker exposure*

Workers can be exposed following application of plant protection products, when entering treated fields or premises or when handling treated plants or plant products on which residues remain. Sufficient information and data must be reported to provide a basis for the selection of appropriate protection measures, including waiting and re-entry periods.

7.2.3.1 *Estimation of worker exposure*

Aim of the estimation

An estimation shall be made, using where available a suitable calculation model, in order to permit an evaluation to be made of the degree of worker exposure likely to arise under the proposed conditions of use.

Circumstances in which required

An estimation of worker exposure must always be completed.

Estimation conditions

An estimation of worker exposure must be made for each crop and task to be carried out.

A first estimation made with the benefit of available data on the exposure likely to arise shall be made on the basis of the assumption that the worker does not use any personal protective equipment.

Where appropriate, a second estimation shall be made on the basis of an assumption that the worker uses that effective and readily obtainable protective equipment which it is feasible for the worker to use.

Where appropriate, a further estimation shall be made using data generated relating to the amounts of dislodgeable residues that occur under the proposed conditions of use.

7.2.3.2 *Measurement of worker exposure*

Aim of the test

The test shall provide sufficient data to permit an evaluation to be made of the degree of worker exposure likely to arise under the proposed conditions of use.

Circumstances in which required

Actual exposure data for relevant exposure route(s) must be reported where risk assessment indicates that a health-based limit value may be exceeded. That will be the case when the results of the estimation of worker exposure provided for under point 7.2.3.1 indicate that -

- the AOELs established in the context of the inclusion of the active substance(s) in Annex I, and/or
- the Limit Values established for the active substance(s) and/or toxicologically relevant compound(s) contained in the plant protection product, in accordance with Council Directive 80/1107/EEC and Council Directive 90/394/EEC,

may be exceeded.

Actual exposure data must also be reported when an appropriate calculation model or appropriate data are not available to permit an estimation to be made as provided for in point 7.2.3.1.

In cases where dermal exposure is the most important exposure route, a dermal absorption test, if not already available, may be a useful alternative test, to provide data to be used in refining the estimation made in accordance with point 7.2.3.1.

Test conditions

The test must be conducted under realistic exposure conditions taking into account the proposed conditions of use.

When measuring exposure to a plant protection product in the air within the breathing space of workers, the requirements for measuring procedures described in Annex IIA to Council Directive 80/1107/EEC of 27 November 1980 on the protection of workers from the risks related to exposure to chemical, physical and biological agents at work must be taken into account

7.3 ***Dermal absorption***

Aim of the test

The test shall provide a measurement of the absorption of the active substance and of toxicologically relevant compounds through the skin.

Circumstances in which required

The study must be conducted when dermal exposure is a significant route and where the risk assessment indicates that a health-based limit value may be exceeded. That will be the case when the results of the estimation or measurement of operator exposure provided for under points 7.2.1.1 or 7.2.1.2 indicate that -

- the AOELs established in the context of the inclusion of the active substance(s) in Annex I, and/or
- the Limit Values established for the active substance(s) and/or toxicologically relevant compound(s) contained in the plant protection product, in accordance with Council Directive 80/1107/EEC and Council Directive 90/394/EEC,

may be exceeded.

Test conditions

In principle data generated through *in vivo* skin absorption testing must be reported. If when the results of the estimation made using *in vivo* skin absorption testing are incorporated in the risk assessment, there nevertheless is an indication of excessive exposure, it may be necessary to perform an *in vitro* comparative absorption study using rat and human skin.

Test guideline

Appropriate elements of OECD Guideline 417 should be used. The results of skin absorption studies conducted with the active substance(s) should be taken into account in designing individual studies.

7.4 ***Available toxicological data relating to non-active substances***

Where available a copy of the notification and the safety data sheet submitted in the context of the Directive of 1967 must be submitted for each formulant. All other available information should be submitted.

8 Residues in or on treated products, food and feed

Introduction

The provisions set out in the introduction to Section 6 of Annex II, apply.

8.1 *Metabolism, distribution and expression of residue in plants or livestock*

Aim of the tests

The objectives of these studies are:

- to provide an estimate of total terminal residues in the relevant portion of crops at harvest following treatment as proposed,
- to quantify the rate of degradation and excretion of the total residue in certain animal products (milk or eggs) and excreta,
- to identify the major components of the total terminal residue in crops and in edible animal products respectively,
- to indicate the distribution of residues between relevant crop parts and between relevant edible animal products respectively,
- to quantify the major components of the residue and to show the efficiency of extraction procedures for these components,
- to generate data on the basis of which a decision can be made as to the need for livestock feeding studies as provided for in point 8.3,
- to provide a basis for a decision as to the definition of and basis for expression of the residue.

Circumstances in which required

Supplementary metabolism studies only need to be performed where it is not possible to extrapolate from data provided for the active substance in accordance with the requirements of points 6.1 and 6.2 of Annex IIA. This might be the case for crops or for livestock for which data were not submitted in the framework of inclusion of the active substance in Annex I or were not necessary for amending the conditions of its inclusion in Annex I or where it could be expected that a different metabolism will occur.

Test conditions

The same provisions as provided under the corresponding paragraphs of points 6.1 and 6.2, of Annex IIA, apply.

8.2 ***Residue trials***

Aim of the tests

The objectives of these studies are:

- to quantify the highest likely residue levels in treated crops at harvest or outloading from store following use in accordance with the proposed good agricultural practice (GAP), and
- to determine, when appropriate, the rate of decline of residues in and/or on crops.

Circumstances in which required

Supplementary residue trials are only required where it is not possible to extrapolate from data obtained on the active substance in accordance with the requirements of point 6.3 of Annex IIA. This might be the case for special formulations, for special application methods or for crops for which data were not submitted in the framework of inclusion of the active substance in Annex I or were not necessary for amending the conditions of its inclusion in Annex 1.

Test conditions

The same provisions as provided under the corresponding paragraphs of point 6.3 pf Annex IIA, apply.

8.3 ***Livestock feeding studies***

Aim of the tests

The objective of these studies is to determine residue levels in products of animal origin that will result from residues in feedingstuffs or fodder crops.

Circumstances in which required

Supplementary feeding studies for the purpose of assessing maximum residue levels for products of animal origin are only required where it is not possible to extrapolate from data obtained on the active substance in accordance with the requirements of point 6.4 of Annex II. This might be the case where additional fodder crops are to be authorized which lead to an increased intake of residues by livestock for which data were not submitted in the framework of inclusion of the active substance in Annex I or were not necessary for amending the conditions of its inclusion in Annex 1.

Test conditions

The same provisions as provided under the corresponding paragraphs of point 6.4 of Annex IIA, apply.

8.4 ***Effects of industrial processing and/or household preparations***

Aim of the tests

The main objectives of these studies are:

- to establish whether or not breakdown or reaction products arise from residues in the raw products during processing which may require a separate risk assessment,
- to determine the quantitative distribution of residues in the various intermediate and end products, and to estimate transfer factors,
- to enable a more realistic estimate to be made of dietary intake of residues.

Circumstances in which required

Supplementary studies only required where it is not possible to extrapolate from data obtained on the active substance in accordance with the requirements of point 6.5 of Annex IIA. This might be the case for crops for which data were not submitted in the framework of inclusion of the active substance in Annex I or were not necessary for amending the conditions of its inclusion in Annex 1.

Test conditions

The same provisions as provided under the corresponding paragraphs of point 6.5 of Annex IIA, apply.

8.5 ***Residues in succeeding crops***

Aim of the test

The objective of these studies is to permit an evaluation to be made as to the residue levels likely to occur in succeeding crops.

Circumstances in which required

Supplementary studies are only required where it is not possible to extrapolate from data obtained on the active substance in accordance with the requirements of point 6.6 of Annex IIA. This might be the case for special formulations, for special application methods or for crops for which data were not submitted in the framework of inclusion of the active substance in Annex I or were not necessary for amending the conditions of its inclusion in Annex 1.

Test conditions

The same provisions as provided under the corresponding paragraphs point 6.6 of Annex IIA, apply.

8.6 ***Proposed maximum residue levels (MRLs) and residue definition***

A full justification for the proposed MRLs must be provided, including, where relevant, full details of the statistical analysis used.

If the metabolism studies submitted in accordance with the provisions of point 8.1 indicate that the residue definition should be changed taking into account the actual residue definition and the necessary judgement as outlined under the corresponding paragraph of point 6.7 of Annex IIA, a re-evaluation of the active substance may be necessary.

8.7 ***Proposed pre-harvest intervals for envisaged uses, or withholding periods or storage periods, in the case of post-harvest uses***

A full justification for the proposals made must be provided.

8.8 ***Estimation of the potential and actual exposure through diet and other means***

Consideration must be given to the calculation of realistic dietary intake levels. This may be done in a step-wise fashion leading to an increasingly realistic prediction of intake. Where relevant, other sources of exposure such as residues arising from the use of medicines or veterinary drugs have to be taken into account.

8.9 ***Summary and evaluation of residue behaviour***

A summary and evaluation of all data presented under point 8 must be provided. It must be carried but and be presented in accordance with the guidance provided by the competent authority. It should include a detailed and critical assessment of the data in the context of relevant evaluative and decision making criteria and guidelines, having particular regard to the risks for man and animals that may or do arise, and the extent, quality and reliability of the data base.

Where metabolism data have been submitted the toxicological significance of any non-mammalian metabolites must be addressed.

A schematic diagram should be prepared of the metabolic pathway in plants and animals with a brief explanation of the distribution and chemical changes involved if metabolism data have been submitted.

9 Fate and behaviour in the environment

Introduction

(i) The information provided, taken together with that for the active substance as provided for in Annex II, must be sufficient to permit an assessment of the fate and behaviour of the plant protection product in the environment, and of the non-target species likely to be at risk from exposure to it.

(ii) In particular, the information provided for the plant protection product, together with other relevant information, and that provided for the active substance, should be sufficient to:

- specify the hazard symbols, the indications of danger, and relevant risk and safety phrases for the protection of the environment, which are to be included on packaging (containers),
- predict the distribution, fate, and behaviour in the environment as well as the time courses involved,
- identify non-target species and populations for which hazards arise because of potential exposure, and
- identify measures necessary to minimize contamination of the environment and impact on non-target species.

(iii) Where radio-labelled test material is used, the provisions of Annex II, Chapter 7, introduction, point (iv) apply.

(iv) Where relevant, tests should be designed and data analysed using appropriate statistical methods.

Full details of the statistical analysis conducted should be reported (*e.g.* all point estimates should be given with confidence intervals, exact p-values should be given rather than stating significant/non significant).

(v) Predicted environmental concentrations in soil (PEC_S), water (PEC_{SW} and PEC_{GW}) and air (PEC_A).

Justified estimates must be made of the expected concentrations of the active substance and relevant metabolites, degradation and reaction products, in soil, ground water, surface water and air, following use as proposed or already occurring. In addition a realistic worst-case estimation must be made.

For the purposes of the estimation of such concentrations the following definitions apply:

Predicted environmental concentrations in soil (PEC_S)

The level of residues, in the top layer of the soil, to which non-target soil organisms may be exposed (acute and chronic exposure).

Predicted environmental concentration in surface water (PEC_{SW})

The level of residues in surface water, to which non-target aquatic organisms may be exposed (acute and chronic exposure).

Predicted environmental concentrations in ground water (PEC_{GW})

The level of residues in ground water.

Predicted environmental concentration in air (PEC_A)

The level of residues in air to which man, animals and other non-target organisms may be exposed (acute and chronic exposure).

For the estimation of these concentrations all relevant information on the plant protection product and on the active substance must be taken into account. A useful approach for these estimations is that provided in the EPPO schemes for environmental risk assessment [63]. Where relevant the parameters provided for in this section should be used.

When models are used for estimation of predicted environmental concentrations they must:

- make a best-possible estimation of all relevant processes involved taking into account realistic parameters and assumptions,
- where possible be reliably validated with measurements carried out under circumstances relevant for the use of the model, and
- be relevant to conditions in the area of use.

The information provided must, where relevant, include that referred to in Annex II, Part A, point 7: and

9.1 ***Fate and behaviour in soil***

Where appropriate, the same provisions relating to the information to be provided on the soil used and on its selection apply as provided for under Annex II, point 7.1.

[63] OEPP/EPPO (1993). Decision-making schemes for the environmental risk assessment of plant protection products. Bulletin OEPP/EPPO, Bulletin 23: 1-154 and Bulletin 24: 1-87

9.1.1 *Rate of degradation in soil*

9.1.1.1 *Laboratory studies*

Aim of the test

Soil degradation studies must provide best possible estimates of the time taken for degradation of 50 and 90% (DT_{50lab} and DT_{90lab}) of the active substance under laboratory conditions.

Circumstances in which required

The persistence and behaviour of plant protection products in soil must be investigated unless it is possible to extrapolate from data obtained on the active substance and relevant metabolites, degradation and reaction products in accordance to the requirements of Annex II, point 7.1.1.2. This extrapolation is, for example, not possible for slow release formulations.

Test conditions

The rate of aerobic and/or anaerobic degradation in soil must be reported.

The duration of the study is normally 120 days except if more than 90% of the active substance is degraded before that period expires.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

9.1.1.2 *Field studies*

Soil dissipation studies

Aim of the test

The soil dissipation studies should provide best-possible estimates of the time taken for dissipation of 50 and 90% (DT_{50f} and DT_{90f}) of the active substance under field conditions. Where relevant, information on relevant metabolites, degradation and reaction products must be collected.

Circumstances in which required.

The dissipation and behaviour of plant protection products in soil must be investigated unless it is possible to extrapolate from data obtained on the active substance and relevant metabolites, degradation and reaction products in accordance to the requirements of Annex II, point 7.1.1.2. This extrapolation is, for example, not possible for slow-release formulations.

Test conditions and test guideline

The same provisions as provided under the corresponding paragraph of Annex II, point 7.1.1.2.2 apply.

Soil residue studies

Aim of the test

Soil residue studies should provide estimates of the soil residue levels at harvest or at time of sowing or planting succeeding crops.

Circumstances in which required

Soil residue studies must be reported unless it is possible to extrapolate from data obtained on the active substance and relevant metabolites, degradation and reaction products in accordance with the requirements of Annex II, point 7.1.1.2.2. This extrapolation is, for example, not possible for slow-release formulations.

Test conditions

The same provisions as provided under the corresponding paragraph of Annex II, point 7.1.1.2.2 apply.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

Soil accumulation studies

Aim of the tests

The tests should provide sufficient data to evaluate the possibility of accumulation of residues of the active substance and of relevant metabolites, degradation and reaction products.

Circumstances in which required

Soil accumulation studies must be reported unless it is possible to extrapolate from data obtained on the active substance and relevant metabolites, degradation and reaction products in accordance with the requirements of Annex II, point 7.1.1.2.2. This extrapolation is, for example, not possible for slow-release formulations.

Test conditions

The same provisions as provided under the corresponding paragraph of Annex II, point 7.1.1.2.2 apply.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

9.1.2 *Mobility in the soil*

Aim of the test

The test should provide sufficient data to evaluate the mobility and leaching potential of the active substance and relevant metabolites, degradation and reaction products.

9.1.2.1 *Laboratory studies*

Circumstances in which required

The mobility of plant protection products in soil must be investigated unless it is possible to extrapolate from data obtained in accordance with the requirements of Annex II, points 7.1.2 and 7.1.3.l. This extrapolation is, for example, not possible for slow-release formulations.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

9.1.2.2 *Lysimeter studies or field leaching studies*

Aim of the tests

The test should provide data on:

- mobility of the plant protection product in soil,
- potential for leaching to ground water,
- potential distribution in soils.

Circumstances in which required

Expert judgement will be necessary to decide whether field leaching studies or lysimeter studies should be carried out, taking into account the results of degradation and mobility studies and the calculated PEC_{GW} value. The type of study to be conducted must be discussed with the competent authorities.

These studies must be performed unless it is possible to extrapolate from data obtained on the active substance and relevant metabolites, degradation and reaction products in accordance to the requirements of Annex II, point 7.1.3. Such extrapolation is, for example, not possible for slow release formulations.

Test conditions

The same provisions as provided for under the corresponding paragraph of Annex II, point 7.1.3.3 apply.

9.1.3 *Estimation of expected concentrations in soil*

PEC_S estimations must relate both to a single application at the highest rate of application for which authorization is sought, and to the maximum number and highest rates of application for which authorization is sought, for each relevant soil tested, and be expressed in terms of mg of active substance and of relevant metabolites, degradation and reaction products per kg of soil.

The factors to be considered in making PEC_S estimations relate to direct and indirect application to soil, drift, run off, and leaching and include processes such as volatilisation, adsorption, hydrolysis, photolysis, aerobic and anaerobic degradation. For the purposes of PEC_S calculations, the bulk density of soils can be assumed to be 1.5 g/cm3 dry weight, while the depth of the soil layer should be assumed to be 5 cm for applications at the soil surface and 20 cm when incorporation in the soil is involved. Where ground cover is present at time of application, it is to be assumed that 50% (minimum) of the applied dose reaches the soil surface unless actual experimental data give more specific information.

Initial, short-term and long-term PEC_S calculations (time weighted averages) must be provided:

Initial:	immediately after application
Short-term:	24 hours, 2 days and 4 days after last application
Long-term:	7, 28, 50 and 100 days after last application, where relevant.

9.2 ***Fate and behaviour in water***

9.2.1 *Estimation of concentrations in ground water*

Ground water contamination routes must be defined taking into account relevant agricultural, plant health, and environmental (including climatic) conditions.

Suitable estimations (calculations) of predicted environmental concentration in ground water PEC_{GW}, of active substance and relevant metabolites, degradation and reaction products, must be submitted.

PEC estimations must relate to the maximum number and highest rates of application, for which authorization is sought.

Expert judgment is required to decide if additional field tests could provide useful information. Before performing these studies the applicant shall seek the agreement of the competent authority on the type of study to be performed.

9.2.2 *Impact on water treatment procedures*

In cases where this information is necessary in the framework of a conditional authorization in accordance with Annex VI, Part C, point 2.5.1.2 (b), the information provided should permit

establishment or estimation of the effectiveness of water treatment procedures (drinking water and sewage treatment), and impact on such procedures.

Before performing any studies the applicant shall seek the agreement of the competent authority on the type of information to be provided.

9.2.3 *Estimation of concentrations in surface water*

Surface water contamination routes must be defined taking into account relevant agricultural, plant health, and environmental (including climatic) conditions.

Suitable estimations (calculations) of predicted environmental concentration in surface water PEC_{SW}, of active substance and relevant metabolites, degradation and reaction products, must be submitted.

PEC estimations must relate to the maximum number and highest rates of application, for which authorization is sought, and be relevant to lakes, ponds, rivers, canals, streams, irrigation/drainage canals and drains.

The factors to be considered in making PEC_{SW} estimations relate to direct application to water, drift, run-off, discharge *via* drains and atmospheric deposition, and include processes such as volatilisation, adsorption, advection, hydrolysis, photolysis, biodegradation, sedimentation and re- suspension.

Initial, short-term and long-term PEC_{SW} calculations relevant to static and slow moving water bodies (time weighted averages) must be provided-

Initial:	immediately after application
Short-term:	24 hours, 2 days and 4 days after last application
Long term:	7, 14, 21, 28, and 42 days after last application, where relevant.

Expert judgment is required to decide if additional field tests could provide useful information. Before performing these studies the applicant shall seek the agreement of the competent authority on the type of study to be performed.

9.3 ***Fate and behaviour in air***

Guidance is under development.

10 **Ecotoxicological studies**

Introduction

(i) The information provided, taken together with that for the active substance(s), must be sufficient to permit an assessment of the impact on non-target species (flora and fauna), of the plant protection product, when used as proposed. Impact can result from single, prolonged or repeated exposure, and can be reversible, or irreversible.

(ii) In particular, the information provided for the plant protection product, together with other relevant information, and that provided for the active substance, should be sufficient to:

- specify the hazard symbols, the indications of danger, and relevant risk and safety phrases for the protection of the environment, to be mentioned on packaging (containers),

- permit an evaluation of the short- and long-term risks for non-target species - populations, communities, and processes as appropriate,
- permit an evaluation of whether special precautions are necessary for the protection of non-target species.

(iii) There is a need to report all potentially adverse effects found during routine ecotoxicological investigations and to undertake and report such additional studies that may be necessary to investigate the mechanisms involved and assess the significance of these effects.

(iv) In general, much of the data relating to impact on non-target species, required for authorization of plant protection products, will have been submitted and evaluated for the inclusion of the active substance(s) in Annex I. The information on fate and behaviour in the environment, generated and submitted in accordance with points 9.1 to 9.3, and on residue levels in plants generated and submitted in accordance with point 8 is central to the assessment of impact on non-target species, in that it provides information on the nature and extent of potential or actual exposure. The final PEC estimations must be adapted as appropriate for the different groups of organisms taking in particular into consideration the biology of the most sensitive species.

The toxicological studies and information submitted in accordance with point 7.1 provide essential information as to toxicity to vertebrate species.

(v) Where relevant, tests should be designed and data should be analysed using appropriate statistical methods. Full details of statistical analyses conducted should be reported (*e.g.* all point estimates should be given with confidence intervals, exact p-values should be given rather than stating significant/non significant).

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

(vii) Where exposure data are necessary to decide whether a study has to be performed, the data obtained in accordance with the provisions of Annex III, point 9 should be used.

For the estimation of exposure of organisms all relevant information on the plant protection product and on the active substance must be taken into account. A useful approach for these estimations is provided in the EPPO/Council of Europe schemes for environmental risk assessment. Where relevant the parameters provided for in this section should be used. Where it appears from available data that the plant protection product is more toxic than the active substance, the toxicity data of the plant protection product must be used for the calculation of relevant toxicity/exposure ratios.

(viii) In the context of the influence that impurities can have on ecotoxicological behaviour, it is essential that for each study submitted, a detailed description (specification) of the material used as provided for under point 1.4, be provided.

(ix) In order to facilitate the assessment of the significance of test results obtained the same strain of each relevant species should, where possible, be used in the various toxicity tests specified.

10.1 ***Effects on birds***

Possible effects on birds must be investigated except where the possibility that birds will be exposed, directly or indirectly, can be ruled out such as for use in enclosed spaces or wound healing treatments.

The acute toxicity/exposure ratio (TER_a), the short term dietary toxicity/exposure ratio (TER_{st}) and the long term dietary toxicity/exposure ratio (TER_{lt}) must be reported, where:

TER_a = LD_{50} (mg active substance/kg body weight) / ETE (mg active substance/kg body weight)

TER_{st} = LC_{50} (mg active substance/kg food) / ETE (mg active substance/kg food)

TER_{lt}) = NOEC (mg active substance/kg food) / ETE (mg active substance/kg food)

where ETE = estimated theoretical exposure.

In the case of pellets, granules or treated seeds the amount of active substance in each pellet, granule or seed must be reported as well as the proportion of the LD_{50} for the active substance in 100 particles and per gram of particles. The size and shape of pellets or granules must be reported.

In the case of baits the concentration of active substance in the bait (mg/kg) must be reported.

10.1.1 *Acute oral toxicity*

Aim of the test

The test should provide, where possible, LD_{50} values, the lethal threshold dose, time courses of response and recovery, the NOEL, and must include relevant gross pathological findings.

Circumstances in which required

The acute oral toxicity of preparations must be reported, where TER_a or TER_{st} for the active substances) in birds are between 10 and 100 or where results from mammal testing provide evidence of a significantly higher toxicity of the preparation compared to the active substance unless it can be justified that it is not likely that birds are exposed to the plant protection product itself.

Test conditions

The study must be conducted on the most sensitive species identified in the studies provided for in Annex II, point 8.1.1 or 8.1.2.

10.1.2 *Supervised cage or field trials*

Aim of the test

The test must provide sufficient data to permit evaluation of the nature and the extent of the risk under practical conditions of use.

Circumstances in which required

Where the TER_a and TER_{st} are > 100 and when there is no evidence of risk from any further study on the active substance (*e.g.* reproduction study) no further testing is required. In other cases, expert judgement is necessary to decide whether there is a need to carry out further studies. This expert judgement will take into account, where relevant, foraging behaviour, repellence, alternative food, actual residue content in the food, persistence of the compound in the vegetation, degradation of the formulated product or treated produce, the amount of predation of the food, acceptance of bait, granules or treated seed and the possibility for bioconcentration.

Where TER_a and $TER_{st} \leq 10$ or $TER_{lt} \leq 5$, cage or field trials must be conducted and be reported unless a final assessment is possible on the basis of studies according to point 10.1.3.

Test conditions

Before performing these studies the applicant must seek the agreement of the competent authority on the type and conditions of the study to be performed.

10.1.3 *Acceptance of bait, granules or treated seeds by birds*

Aim of the test

The test should provide sufficient data to evaluate the possibility of consumption of the plant protection product or plant products treated with it.

Circumstances in which required

In the case of seed dressings, pellets, baits and preparations which are granules and where $TER_a. \leq 10$, acceptability (palatability) tests must be conducted.

10.1. 4 *Effects of secondary poisoning*

Expert judgement is required to decide whether the effects of secondary poisoning should be investigated.

10.2 ***Effects on aquatic organisms***

Possible effects on aquatic species must be investigated except where the possibility that aquatic species will be exposed can be ruled out.

TER_a and TER_{lt} must be reported, where:

TER_a = acute LC_{50} (mg active substance/L) / realistic worst case PEC_{SW} (initial or short-term, in mg active substance/L)

TER_{lt} = chronic NOEC (mg active substance/L) / long term PEC_{SW} (mg active substance/L)

10.2.1 *Acute toxicity to fish, aquatic invertebrates or effects on algal growth*

Circumstances in which required

In principle tests should be carried out on one species from each of the three groups of aquatic organisms as referred to in Annex II, point 8.2 (fish, aquatic invertebrates and algae) in cases where the plant protection product itself can contaminate water. However where the available information permits the conclusion that one of these groups is clearly more sensitive, tests on only the most sensitive species of the relevant group have to be performed.

The test must be performed where:

- the acute toxicity of the plant protection product cannot be predicted on the basis of the data for the active substance which is especially the case if the formulation contains two or more active substances or contains formulants such as solvents, emulgators, surfactants, dispersants or fertilizers which can increase toxicity in comparison with the active substance, or
- the intended use includes direct application on water,

unless suitable studies referred to under point 10.2.4 are available.

Test conditions and test guidelines

The relevant provisions of the corresponding paragraphs of Annex II, points 8.2.1, 8.2.4 and 8.2.6 apply.

10.2.2 *Microcosm or mesocosm study*

Aim of the test

The tests must provide sufficient data to permit evaluation of essential impact on aquatic organisms under field conditions.

Circumstances in which required

Where $TER_a \leq 10$ or where $TER_{lt} \leq 10$, expert judgement must be used to decide whether a microcosm or mesocosm study is appropriate. This judgement will take into account the results of any additional data over and above those required in accordance with the provisions of Annex II, point 8.2 and point 10.2.1.

Test conditions

Before performing these studies the applicant shall seek the agreement of the competent authority on the specific aims of the study to be performed and consequently on the type and conditions of the study to be performed.

The study should include at least the highest likely exposure rate, whether from direct application, drift, drainage or run-off. The duration of the study must be sufficient to permit evaluation of all effects.

Test guideline

Appropriate guidelines are included in:

SETAC - Guidance document on testing procedures for pesticides in freshwater mesocosms / Workshop Huntingdon, 3 and 4 July 1 99 1,

or

Freshwater field tests for hazard assessment of chemicals - European Workshop on Freshwater Field Tests (EWOFFT).

10.2.3 *Residue data in fish*

Aim of the test

The test must provide sufficient data to evaluate the potential for occurrence of residues in fish.

Circumstances in which required

In general relevant data are available from bioconcentration studies in fish.

Where bioconcentration has been observed in the study performed in accordance with Annex II, point 8.2.3, expert judgement is required to decide whether a long- term microcosm or mesocosm study is necessary out in order to establish the maximum residues likely to be encountered.

Test guideline

SETAC - Guidance document on testing procedures for pesticides in freshwater mesocosms / Workshop Huntingdon, 3 and 4 July 1991.

10. 2.4 *Additional studies*

The studies referred to in Annex II, points 8.2.2 and 8.2.5 may be required for particular plant protection products where it is not possible to extrapolate from data obtained in the corresponding studies on the active substance.

10.3 ***Effects on terrestrial vertebrates other than birds***

Possible effects on wild vertebrate species must be investigated except where it can be justified that it is not likely that terrestrial vertebrates other than birds are exposed, directly or indirectly.
TER,,, TER,,, and TER,, must be reported, where:

TER_a, TER_{st} and TER_{lt} must be reported, where:

TER_a = LD_{50} (mg active substance/kg body weight) / ETE (mg active substance/kg body weight)

TER_{st} = sub chronic NOEL (mg active substance/kg food) / ETE (mg active substance/kg food)

TER_{lt}) = chronic NOEL (mg active substance/kg food) / ETE (mg active substance/kg food)

where ETE = estimated theoretical exposure.

In principle the evaluation sequence for the assessment of risks to such species is similar to that for birds. In practice it is not often necessary to perform further testing as the studies conducted in accordance with the requirements of Annex II, point 5 and Annex III, point 7 provide the required information.

Aim of the test

Testing must provide sufficient information to evaluate the nature and the extent of risks for terrestrial vertebrates other than birds under practical conditions of use.

Circumstances in which required

Where TER_a and $TER_{st} > 100$ and where there is no evidence of risk from any further study, no further testing is required. In other cases, expert judgement is necessary to decide whether or not there is a need to carry out further studies. This expert judgement must take into account, where relevant, foraging behaviour, repellence, alternative food, actual residue content in the food, persistence of the compound in the vegetation, degradation of the formulated product or treated produce, the amount of predation of the food, acceptance of bait, granules or treated seed and the possibility for bioconcentration.

Where TER_a and $TER_{st} \leq 10$ or $TER_{lt} \leq 5$, cage or field trials or other appropriate studies must be reported.

Test conditions

Before performing these studies the applicant must seek agreement of the competent authority on the type and conditions of the study to be performed and whether the effects of secondary poisoning should be investigated.

10.4 ***Effects on bees***

Possible effects on bees must be investigated except where the product is for exclusive use in situations where bees are not likely to be exposed such as:

- food storage in enclosed spaces,
- non-systemic seed dressings,
- non-systemic preparations for application to soil,
- non-systemic dipping treatments for transplanted crops and bulbs,
- wound sealing and healing treatments,
- rodenticidal baits,
- use in glasshouses without pollinators.

The hazard quotients for oral and contact exposure (Q_{HO} and Q_{HC}), must be reported:

Q_{HO} = dose / oral LD_{50} (µg active substance per bee)

Q_{HC} = dose / contact LD_{50} (µg active substance per bee)

where

dose = the maximum application rate, for which authorization is sought, in g of active substance per hectare.

10.4.1 *Acute oral and contact toxicity*

Aim of the test

The test should provide LD_{50} values (by oral and contact exposure).

Circumstances in which required

Testing is required if:

- the product contains more than one active substance,
- the toxicity of a new formulation cannot be reliably predicted to be either the same or lower than a formulation tested according to the provisions of Annex II, point 8.3.1.1 or of this point.

Test guideline

The test must be carried out in accordance with EPPO Guideline 170.

10.4.2 *Residue test*

Aim of the test

The test should provide sufficient information to permit evaluation of possible risks to foraging bees from residual traces of plant protection products remaining on crops.

Circumstances in which required

Where $Q_{HC} \geq 50$, expert judgement is required to decide whether the effect of residues must be determined unless there is evidence that there are no significant residual traces remaining on crops which could affect foraging bees or unless sufficient information is available from cage, tunnel or field tests.

Test conditions

The median lethal time (LT_{50}) (in hours) following 24 hour exposure to residues on leaves aged during eight hours must be determined, and reported. Where LT_{50} is more than eight hours, no further testing is required.

10.4.3 *Cage tests*

Aim of the test

The test should provide sufficient information to permit evaluation of possible risks from the plant protection product for bee survival and behaviour.

Circumstances in which required

Where Q_{HO} and Q_{HC} are < 50, further testing is not required except if significant effects are observed in the bee brood feeding test or if there are indications of indirect effects such as delayed action or modification of bee behaviour. In such cases cage and/or field tests shall be carried out.

Where Q_{HO} and Q_{HC} are > 50, cage and/or field testing is required.

Where field testing is conducted and reported in accordance with point 10.4.4, it is not necessary to conduct cage tests. However, cage tests where conducted, must be reported.

Test conditions

Testing should be carried out using healthy bees. If bees have been treated, *e.g.* with a varroacide, it is necessary to wait for four weeks before using the colony.

Test guideline

Testing must be conducted in accordance with EPPO Guideline 170.

10.4.4 *Field tests*

Aim of the test

The test should provide sufficient information to permit evaluation of possible risks from the plant protection product on bee behaviour, colony survival and development.

Circumstances in which required

Field tests must be conducted where on the basis of expert judgement, taking into account the proposed manner of use and the fate and behaviour of the active substance, significant effects are observed in cage testing.

Test conditions

The test should be carried out using healthy honeybee colonies of similar natural strength. If bees have been treated, *e.g.* with a varroacide, it is necessary to wait for four weeks before using the colony. The tests must be conducted under conditions reasonably representative of the proposed use.

Special effects (larval toxicity, long residual effect, disorienting effects on bees) identified in the field tests may require further investigation using specific methods.

Test guideline

Testing must be conducted in accordance with EPPO Guideline 170.

10.4.5 *Tunnel tests*

Aim of the test

The test should provide sufficient information to permit evaluation of the impact on bees resulting from feeding on contaminated honey dew or flowers.

Circumstances in which required

Where it is not possible to investigate certain effects in cage or field trials, a tunnel test should be carried out, *e.g.* in the case of plant protection products intended for control of aphids and other sucking insects.

Test conditions

The test should be carried out using healthy bees. If bees have been treated, *e.g.* with a varroacide, it is necessary to wait for four weeks before using the colony.

Test guideline

Testing must be conducted in accordance with EPPO Guideline 170.

10.5 ***Effects on arthropods other than bees***

The effects of plant protection products on non-target terrestrial arthropods (*e.g.* predators or parasitoids of harmful organisms) must be investigated. The information obtained for these species can also be used to indicate the potential for toxicity to non-target species inhabiting the same environment.

10.5.1 *Laboratory, extended laboratory and semi-field tests*

Aim of the test

The test should provide sufficient information to permit evaluation of the toxicity of the plant protection product for selected arthropod species that are relevant to the intended use of the product.

Circumstances in which required

Testing is not required where severe toxicity (> 99% effect on the organisms compared to control) can be predicted from relevant available data or where the plant protection product is for exclusive use in situations where non-target arthropods are not exposed such as:

- food storage in enclosed spaces,
- wound sealing and healing treatments,
- rodenticidal baits.

Testing is required when significant effects on the organisms in comparison with the control are reported in the laboratory tests at the maximum recommended dose, conducted in accordance with the requirements of Annex II, point 8.3.2. Effects on a particular test species are considered to be significant when they exceed the threshold values specified in the EPPO schemes for environmental risk assessment unless species-specific threshold values are defined in the respective test guidelines.

Testing is also required if:

- the product contains more than one active substance,
- the toxicity of a new formulation cannot be reliably predicted to be either the same or lower than a formulation tested in accordance with the provisions of Annex II, point 8.3.2 or of this point,
- on the basis of the proposed manner of use or on the basis of fate and behaviour continued or repeated exposure can be anticipated,
- there is a significant change in the proposed use, *e.g.* from arable crops to orchards and species relevant to the new use have not previously been tested,
- there is an increase in the recommended application rate, above that previously tested under Annex II.

Test conditions

Where significant effects were observed in the studies performed in accordance with the requirements of Annex II, point 8.3.2, or in the case of change of use such as from arable crops to orchards, the toxicity of two additional relevant species must be investigated and be reported. These must be different to the relevant species already tested in accordance with Annex II, point 8.3.2.

For a new mixture or formulation, toxicity should initially be assessed using the two most sensitive species as identified in studies already performed for which the threshold values were exceeded but effects still remain below 99%. This will enable a comparison to be made; if it is significantly more toxic two species relevant to its proposed use must be tested.

Testing must be conducted at a rate equivalent to the maximum rate of application for which authorization is sought. A sequential testing approach should be adopted, *i.e.* laboratory, and if necessary extended laboratory and/or semi-field.

Where there will be more than one application per season, the product should be applied at twice the recommended application rate unless this information is already available from studies performed in accordance with Annex II, point 8.3.2.

Where on the basis of the proposed manner of use or on the basis of data concerning fate and behaviour, continued or repeated exposure can be anticipated (such as the product is to be applied more than three times per season with a re-application interval of 14 days or less), expert judgement is required to determine whether or not further testing is required, beyond initial laboratory testing, and which will reflect the proposed use pattern. These tests may be performed in the laboratory or under semi-field conditions. When the test is performed in the laboratory a realistic substrate such as plant material or a natural soil should be used. However it may be more appropriate to carry out field tests.

Test guideline

Where relevant, testing should be carried out in accordance with appropriate guidelines that satisfy at least the requirements for testing included in the SETAC - Guidance document on regulatory testing procedures for pesticides with non-target arthropods.

10.5.2 *Field tests*

Aim of the test

The tests should provide sufficient information to permit evaluation of the risk of the plant protection product for arthropods under field conditions.

Circumstances in which required

Where significant effects are seen following laboratory and semi-field testing, or where on the basis of the proposed manner of use or on the basis of fate and behaviour data, continued or repeated exposure can be anticipated, expert judgement is required to determine whether more extensive testing is necessary to permit an accurate risk assessment.

Test conditions

The tests must be conducted in accordance with the proposed recommendations for use under representative agricultural conditions, providing a realistic worst case study.

A toxic standard should be included in all tests.

Test guideline

Where relevant, testing should be carried out in accordance with appropriate guidelines that satisfy at least the requirements for testing included in the SETAC - Guidance document on regulatory testing procedures for pesticides with non-target arthropods.

10.6 ***Effects an earthworms and other soil non-target macro-organisms, believed to be a risk***

10.6.1 *Effects on earthworms*

Possible impact on earthworms must be reported except where it can be justified that it is not likely that earthworms are exposed, directly or indirectly.

TER_a and TER_{lt} must be reported, where:

TER_a = acute LC_{50} (mg active substance/kg) / realistic worst case PEC_S (initial or short-term, in mg active substance/kg)

TER_{lt} = chronic NOEC (mg active substance/kg) / long term PEC_S (mg active substance/kg)

10.6.1.1 *Acute toxicity tests*

Aim of the test

The test should provide and estimate of the LC_{50}, where possible the highest concentration causing no mortality and the lowest concentration causing 100% mortality and must include observed morphological and behavioural effects.

Circumstances in which required

These studies are only required where:

- the product contains more than one active substance,
- the toxicity of a new formulation cannot be reliably predicted from the formulation tested in accordance with the provisions of Annex II, point 8.4 or of this point.

Test guideline

The tests must be conducted in accordance with OECD Method 207.

10.6.1.2 *Tests for sub lethal effects*

Aim of the test

The test should provide an estimate of the NOEC and identify effects on growth, reproduction and behaviour.

Circumstances in which required

These studies are only required where:

- the product contains more than one active substance,
- the toxicity of a new formulation cannot be reliably predicted on the basis of the formulation tested in accordance with the provisions of Annex II, point 8.4 or of this point,
- there is an increase in the recommended application rate, above that previously tested.

Test conditions

The same provisions as those specified in the corresponding paragraphs of Annex II, point 8.4.2 apply.

10.6.1.3 *Field studies*

Aim of the test

The test should provide sufficient data to permit evaluation of effects on earthworms under field conditions.

Circumstances in which required

Where $TER_{lt} < 5$, a field study to determine effects under practical field conditions must be conducted and reported.

Expert judgement is required to decide whether the residue content of earthworms should be investigated.

Test conditions

Fields selected must have a reasonable earthworm population.

The test must be carried out at the maximum proposed application rate. A toxic reference product must be included in the test.

10.6.2 *Effects on other soil non-target macro-organisms*

Aim of the test

The test should provide sufficient data to permit evaluation of the impact of the plant protection product on macro-organisms that contribute to the breakdown of dead plant and animal organic matter.

Circumstances in which required

Testing is not required where in accordance with the results of testing pursuant to Annex III, point 9.1, it is evident that DT_{90} values are less than 100 days, or the nature and manner of use of the plant protection product are such that exposure does not occur or when data from studies on the active substance performed in accordance with the provisions of Annex II, points 8.3.2, 8.4 and 8.5 indicate that there is no risk for soil macrofauna, earthworms or soil microflora.

Impact on organic matter breakdown must be investigated and reported, where the DT_{90f} values determined in field dissipation studies (point 9.1) are > 365 days.

10.7 ***Effects on soil non-target micro-organisms***

10.7.1 *Laboratory testing*

Aim of the test

The test should provide sufficient data to permit evaluation of the impact of the plant protection product on soil microbial activity in terms of nitrogen transformation and carbon mineralization.

Circumstances in which required

Where the DT_{90f} values determined in field dissipation studies (point 9.1) are > 100 days, impact on soil non-target micro-organisms must be investigated through laboratory testing. Testing is, however, not required if in the studies performed in accordance with the provisions of Annex II, point 8.5, deviations from control values in terms of metabolic activity of the microbial biomass after 100 days are < 25%, and such data are relevant to the uses, nature and properties of the particular preparation to be authorized.

Test guideline

SETAC - Procedures for assessing the environmental fate and ecotoxicity of pesticides.

10.7.2 *Additional testing*

Aim of the test

The test should provide sufficient data to permit evaluation of the impact of the plant protection product under field conditions on microbial activity.

Circumstances in which required

Where at the end of 100 days, measured activity deviates by more than 25% from the control, in laboratory tests, further testing in the laboratory, under glass and/or in the field may be necessary.

10.8 ***Available data from biological primary screening in summary form***

A summary of available data from preliminary tests used to assess the biological activity and dose range finding whether positive or negative, which provides information with respect to possible impact on non-target species, both flora and fauna, must be provided, together with a critical assessment as to its relevance to potential impact on non-target species.

11 Summary and evaluation of Points 9 and 10

A summary and evaluation of all data presented in accordance with points 9 and 10, prepared in accordance with the relevant guidelines specified in the **Fourth Schedule**, must be provided. It should include a detailed and critical assessment of those data in the context of relevant evaluative and decision making criteria and guidelines, with particular reference to the risks for the environment and non-target species that may or do arise, and the extent, quality and reliability of the data base. In particular the following issues should be addressed:

- prediction of distribution and fate in the environment, and the time courses involved,
- identification of non-target species and populations at risk, and prediction of the extent of potential exposure,
- evaluation as to the short- and long-term risks for non target species - populations, communities, and processes - as appropriate,
- evaluation as to the risk of fish kills, and fatalities in large vertebrates, or terrestrial predators, regardless of effects at population or community level, and
- identification of precautions necessary to avoid or minimize contamination of the environment, and for the protection of non-target species.

12 Further information

12.1 ***Information on authorization in other countries***

12.2 ***Information on established maximum residue limits (MRLs) in other countries***

12.3 ***Proposals including justification for the classification and labelling proposed in accordance with the Regulations of 2001***

- Hazard symbol(s)
- Indications of danger
- Risk phrases
- Safety phrases

12.4 ***Proposals for risk and safety phrases in accordance with Regulation 24 (3) (h) and (i) and the proposed label***

12.5 ***Specimens of proposed packaging***

PART B

Preparations of micro-organisms

Introduction

(i) The data and information required for the authorization of plant protection products containing micro-organisms including viruses are set out hereunder.

For the purposes of Part B, of this Annex, the term micro-organism is defined as:

"*a microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material*"

The definition applies to, but is not limited to, bacteria, fungi, protozoa, viruses and viroids.

(ii) Where relevant, data must be analysed using appropriate statistical methods. Full details of the statistical analysis conducted must be reported (*e.g.* all point estimates must be given with confidence intervals, exact p-values must be given rather than stating significant/non significant).

(iii) Pending the adoption of internationally accepted guidelines, the information required must be generated using test guidelines accepted by the competent authority (*e.g.* US EPA guideline); where appropriate test guidelines described in Annex II, Part A, should be adapted such that they are appropriate for micro-organisms. Testing should include viable and, if appropriate, non-viable micro-organisms, and a blank control.

(iv) Whenever a study involves use of different doses, the relationship between dose and adverse effect must be reported.

(v) Where testing is carried out, a detailed description (specification) of the material used and its impurities, in accordance with the provisions of point 1.4 of Section 1 must be provided.

(vi) Extrapolation on the basis of the results of testing conducted in accordance with Part B of Annex II, may be acceptable, where the possible effects of formulants and other components, on pathogenicity and infectivity are reported.

1 **Identity of the plant protection product**

The information provided, taken together with that provided for the micro-organism(s), must be sufficient to precisely identify and define preparations. The information and data referred to, unless otherwise specified, are required for all plant protection products. It is important that factors that could alter the properties of the plant protection product in comparison to the micro-organism as such, be identified.

1.1 ***Applicant***

The name and address of the applicant (permanent community address) must be provided, as must the name, position, telephone and telefax number of the appropriate person to contact.

Where, in addition, the applicant has an office, agent or representative in the territory of the State, the name and address of the local office, agent or representative must be provided, as must the name, position, telephone and telefax number of the appropriate person to contact.

1.2 ***Manufacturer of the preparation and the micro-organism(s)***

The name and address of the manufacturer of the preparation and of each micro-organism in the preparation must be provided as must the name and address of each manufacturing plant in which the preparation and micro-organism are manufactured.

A contact point (preferable a central contact point, to include name, telephone and telefax numbers) must be provided for each manufacturer.

If the micro-organism originates from a producer from which data according to Annex II, part B, had not been submitted previously, detailed information on the name and species description, as specified in point 1.3 of Part B of Annex II, and on impurities, as specified in point 1.4 of Part B of Annex II, must be provided.

1.3 ***Trade name or proposed trade name, and manufacturer's development code number of the preparation if appropriate***

All former and current trade names and proposed trade names and development code numbers of the preparation as well as the current names and numbers must be provided. Where trade names and code numbers referred to, relate to similar but different preparations (possibly obsolete), full detail of the differences must be provided. (The proposed trade name may not give rise to confusion with the trade names of plant protection products already authorized.)

1.4 ***Detailed quantitative and qualitative information on the composition of the preparation***

(i) Each micro-organism in the preparation must be identified and named at the species level. Each such micro-organism must be deposited at an internationally recognised culture collection and have been given an accession number, details of which must be reported. The scientific name of the micro-organism must be stated, as well as its group assignment (*e.g.* bacteria, virus, *etc.*) and taxonomic grouping (*e.g.* family, genus, species, strain, serotype, pathovar) or other denomination relevant to the micro-organism, must be reported. In addition, the development stage of the micro-organism (*e.g.* spores, mycelium) in the marketed product must be reported.

(ii) For preparations the following information must be reported -

- content of the micro-organism(s) in the plant protection product and the content of the micro-organism in the material used for manufacturing plant protection products. The maximum, minimum and nominal content of the viable and non-viable material must be provided,
- content of formulants,
- content of other components (*e.g.* by-products, condensates, culture medium, *etc.*) and contaminating micro-organisms, derived from the production process.

Concentrations must be expressed for chemicals -

- for preparations that are solids, aerosols, volatile liquids (maximum boiling point 50 °C) or viscous liquids (lower limit 1 PA at 20 °C), as a percentage by weight,
- for other liquids, as a percentage by weight and in grams per litre at 20 °C, and
- for gasses, as a percentage by volume, and

in the case of micro-organisms in other appropriate terms (*e.g.* number of active units per volume or weight or other manner appropriate for micro-organisms).

(iii) Formulants must where possible, be identified either by their chemical name as given in Annex I to the Directive of 1967, or, if not included in that Directive, in accordance with both IUPAC and CA nomenclature. Their structure or structural formula must be provided. For each component of formulants the relevant EEC (EINECS or ELINCS) number and CAS number where they exist, must be provided. Where the information provided does not fully identify a formulant, an appropriate specification must be provided. The trade name of formulants, where they exist, must also be provided.

(iv) For formulants their function must be given -

adhesive (sticker)	dye	repellent
antifoaming agent	emetic	safener
antifreeze	emulsifier	solvent
binder	fertilizer	stabiliser
buffer	odorant	synergist
carrier	perfume	thickener
deodorant	preservative	wetting agent
dispersing agent	propellant	miscellaneous (specify)

(v) Identification of contaminating micro-organisms and other components derived from production process.

Contaminating micro-organisms must be identified in accordance with the provisions of point 1.3 of Part B of Annex I. Chemical contaminants (inert components, by-products, *etc.*) must be identified in accordance with the provisions of point 1.10 of Part A of Annex II.

Where the information provided does not fully identify a component (*viz.* condensates, culture medium, *etc.*), detailed information on their composition must be provided for each such component.

1.5 ***Physical state and nature of the preparation***

The type and code of the preparation must be designated according to the "Catalogue of pesticide formulation types and international coding system (GIFAP Technical Monograph No 2, 1989)"

Where a particular preparation is not defined precisely in that publication a full description of the physical nature and state of the preparation must be provided, together with a proposal for a suitable description of the type of preparation and a proposal for its definition.

1.6 ***Function***

The biological function of the preparation must be specified from among the following -

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

2 Physical, chemical and technical properties of the plant protection product

The extent to which plant protection products for which authorization is sought, comply with relevant FAO specifications as agreed by the Group of Experts on Pesticide Specifications, of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements and Application Standards, must be stated. Divergences from FAO specifications must be described in detail, and justified.

2.1 *Appearance (colour and odour)*

A description of both the colour and odour, if any, and the physical state of the preparation, must be provided.

2.2 *Storage stability and shelf-life*

2.2.1 *Effects of light, temperature and humidity on technical characteristics of the plant protection product*

(i) The physical and biological stability of the preparation at the recommended storage temperature and information on the growth of contaminating micro-organisms must be determined and reported. The conditions under which the test was performed must be justified.

(ii) In addition, in the case of liquid preparations, the effect of low temperatures on physical stability, must be determined in accordance with CIPAC Methods MT 39, MT 48, MT 51 or MT 54 as appropriate and be reported.

(iii) The shelf life of the preparation at the recommended storage temperature must be reported. Where shelf life is less than two years, the shelf life in months, with appropriate temperature specifications must be reported. GIFAP Monograph No 17 contains useful information on such testing.

2.2.2 *Other factors affecting stability*

The effects of exposure to air, of packaging type, *etc*., on product stability must be explored and be reported.

2.3 *Explosivity and oxidizing properties*

Explosivity and oxidising properties must be determined and be reported, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.3.1 The explosive properties of preparations must be determined in accordance with EEC Method A 14 and be reported. Where available thermodynamic information establishes beyond reasonable doubt, that the preparation is incapable of exothermic reaction, it is sufficient to provide that information as a justification for not determining the explosive properties of the preparation.

2.3.2 The oxidizing properties of preparations that are solids, must be determined in accordance with EEC Method A 17 and be reported. For other preparations the method used must be justified.

Oxidizing properties do not have to be determined if it can be shown without reasonable doubt, on the basis of thermodynamic information, that the preparation is incapable of reacting exothermically with combustible materials.

2.4 ***Flash point and other indications of flammability or spontaneous ignition***

Flash point and flammability must be determined and be reported, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

The flash point of liquids that contain flammable solvents, must be determined in accordance with EEC Method A 9 and be reported. The flammability of solid preparations and gasses must be determined in accordance with EEC Method A 10, A 11 or A 12, as appropriate, and be reported. The auto-flammability of preparations, determined in accordance with EEC Method A 15 or A 16 as appropriate, and/or, where necessary, in accordance with the UN-Bowes-Cameron-Cage-Test (UN-Recommendations on the Transport of Dangerous Goods, Chapter 14, Nr.14.3.4), must be reported.

2.5 ***Acidity, alkalinity and if necessary pH value***

Acidity, alkalinity and pH must be determined and be reported unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.5.1 In the case of preparations that are acidic (pH < 4) or alkaline (pH > 10) the acidity or alkalinity and the pH value must be determined in accordance with CIPAC Method MT 31 and MT 75 respectively, and be reported.

2.5.2 Where relevant (if to be applied as aqueous dilution) the pH of a 1 % aqueous dilution, emulsion or dispersion of the preparation, must be determined in accordance with CIPAC Method MT 75 and be reported.

2.6 ***Viscosity and surface tension***

Viscosity and surface tension must be determined and reported, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.6.1 In the case of liquid preparations for Ultra Low Volume use (ULV) kinematic viscosity must be determined in accordance with OECD Test Guideline 14 and be reported.

2.6.2 For non newtonian liquids viscosity must be determined and reported together with the test conditions.

2.6.3 In the case of liquid preparations surface tension must be determined in accordance with EEC Method A 5 and be reported.

2.7 ***Technical characteristics of the plant protection product***

The technical characteristics of the preparation must be determined and be reported to permit assessment of its acceptability. Where testing is necessary, it must be conducted at temperatures compatible with survival of the micro-organism.

2.7.1 *Wettability*

The wettability of solid preparations that are diluted for use (e.g. wettable powders and water dispersible granules), must be determined and reported according to CIPAC Method MT 53.3.

2.7.2 *Persistent foaming*

The persistence of foaming of preparations to be diluted with water, must be determined according to CIPAC Method MT 47 and be reported.

2.7.3 *Suspensibility and suspension stability*

2.7.3.1 The suspensibility of water dispersible products (*e.g.* wettable powders, water dispersible granules, suspension concentrates) must be determined in accordance with CIPAC Method MT 15, MT 161 or MT 168, as appropriate, and be reported.

2.7.3.2 The spontaneity of dispersion of water dispersible products (*e.g.* suspension concentrates and water dispersible granules) must be determined in accordance with CIPAC Methods MT 160 or MT 174, as appropriate, and be reported.

2.7.4 *Dry sieve test and wet sieve test*

In order to ensure that dustable powders have a suitable particle size distribution for ease of application, a dry sieve test must be conducted in accordance with CIPAC Method MT 59.1 and be reported.

In the case of water dispersible products, a wet sieve test must be conducted in accordance with CIPAC Method MT 59.3 or MT 167, as appropriate, and be reported.

2.7.5 *Particle size distribution (dustable and wettable powders, granules), content of dust/fines (granules), attrition and friability (granules)*

2.7.5.1 The size distribution of particles in the case of powders, must be determined in accordance with OECD Method 110 and be reported.

The nominal size range of granules for direct application must be determined in accordance with CIPAC MT 58.3 and for water dispersible granules and in accordance with CIPAC MT 170, and be reported.

2.7.5.2 The dust content of granular preparations, must be determined in accordance with CIPAC Method MT 171 and be reported. If relevant for operator exposure the particle size of dust must be determined in accordance with OECD Method 110 and be reported.

2.7.5.3 The friability and attrition characteristics of granules, must be determined and reported once internationally agreed methods are available. Where relevant data are available they must be reported together with details of the method used.

2.7.6 *Emulsifiability, Re-emulsifiability, emulsion stability*

2.7.6.1 The emulsifiability, emulsion stability and re-emulsifiability of preparations that form emulsions, must be determined in accordance with CIPAC Methods MT 36 or MT 173, as appropriate, and be reported.

2.7.6.2 The stability of dilute emulsions and of preparations that are emulsions, must be determined in accordance with CIPAC Method MT 20 or MT 173, as appropriate, and be reported.

2.7.7 *Flowability, pourability (rinsability) and dustability*

2.7.7.1 The flowability of granular preparations must be determined in accordance with CIPAC Method MT 172 and be reported.

2.7.7.2 The pourability (including rinsed residue) of suspensions (*e.g.* suspension concentrates, suspo-emulsions), must be determined in accordance with CIPAC Method MT 148 and be reported.

2.7.7.3 The dustability of dustable powders must be determined in accordance with CIPAC Method MT 34 or another suitable method and be reported.

2.8 ***Physical, chemical and biological compatibility with other products including plant protection products with which its use is to be authorized***

2.8.1 *Physical compatibility*

The physical compatibility of recommended tank mixes must be determined and be reported.

2.8.2 *Chemical compatibility*

The chemical compatibility of recommended tank mixes must be determined and be reported except where examination of the individual properties of the preparations establishes beyond reasonable doubt that there is no possibility of reaction taking place. In such cases it is sufficient to provide that information as justification for not determining chemical compatibility.

2.8.3 *Biological compatibility*

The biological compatibility of recommended tank mixes must be determined and be reported. Effects on the activity of the micro-organism (*e.g.* antagonism, fungicidal effects) following mixing with other micro-organisms or chemicals must be described. Possible interactions under expected condition of use, that may affect the efficacy of the plant protection product where it is to be applied with other chemical products must be investigated and be reported. Where appropriate, intervals between application of the biological plant protection product and chemical products should be specified, where appropriate to avoid loss of efficacy.

2.9 ***Adherence and distribution to seeds***

In the case of preparations for seed treatment, both distribution and adhesion must be investigated and be reported; in the case of distribution in accordance with CIPAC Method MT 175.

2.10 ***Summary and evaluation of data presented under points 2.1 to 2.9***

3 Data on application

3.1 *Field of use envisaged*

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

Field use
- Agriculture
- Horticulture
- Forestry
- Viticulture

Protected crops

Amenity

Weed control on non-cultivated areas

Home gardening

House plants

Plant products storage practice

Other (specify)

3.2 *Mode of action*

The mechanism by which uptake of the micro-organism, or its metabolites (especially toxins) occurs (*e.g.* contact, stomach, inhalation) must be described as must the type of controlling action (*e.g.* fungitoxic, fungistatic action, nutrient competition, *etc.*).

It must also be stated whether or not the product is translocated in plants and, where relevant, if such translocation is apoplastic, symplastic or both.

3.3 *Details of intended use*

Details of the intended use, *e.g.* types of harmful organisms controlled and/or plants or plant products to be protected, must be provided.

The recommended intervals between application of the plant protection product and plant protection products containing chemical active substances must be provided. Alternatively, a list of chemical active substances contained in plant protection products that should not be applied together with the plant protection product containing a micro-organism can be provided.

3.4 *Application rate*

For each method of application and each use, the rate of application per unit (ha, m^2, m^3) treated, in terms of g or kg or L for the preparation and in terms of appropriate units for the micro-organism, must be provided.

Application rates must normally be expressed in g or kg/ha or in kg/m^3 and where appropriate in g or kg/tonne; for protected crops and home gardening use, rates must be expressed in g or $kg/100m^2$ or g or kg/m^3.

3.5 ***Content of micro-organism in material used (e.g. in the diluted spray, baits or treated seed)***

The content of micro-organism must be reported, as appropriate, in terms of number of active unit/ml or g or any other relevant unit.

3.6 ***Method of application***

The method of application proposed must be described fully, indicating the type of equipment to be used, if any, as well as the type and volume of diluent to be used per unit of area or volume.

3.7 ***Number and timing of applications and duration of protection***

The maximum number of applications to be used and their timing must be reported. Where relevant the growth stages of the crop or plants to be protected and the development stages of the harmful organisms, must be indicated. Where possible and necessary the interval between applications, in days, must be stated.

The duration of protection afforded both by each application and by the maximum number of applications to be used, must be indicated.

3.8 ***Necessary waiting periods or other precautions to avoid phytopathogenic effects on succeeding crops***

Where relevant, minimum waiting periods between last application and sowing or planting of succeeding crops, that are necessary to avoid phytopathogenic effects on succeeding crops, must be stated, and follow from the data provided in accordance with point 6.6.

Limitations on choice of succeeding crops, if any, must be stated.

3.9 ***Proposed instructions for use***

The proposed instructions for use of the preparation, to be printed on labels and leaflets, must be provided.

4 Further information on the plant protection product

4.1 *Packaging and compatibility of the preparation with proposed packaging materials*

4.1.1 Packaging to be used must be fully described and specified in terms of the materials used, manner of construction (*e.g.* extruded, welded *etc.*), size and capacity, size of opening, type of closure and seals. It must be designed in accordance with the criteria and guidelines specified in the FAO "Guidelines for the Packaging of Pesticides".

4.1.2 The suitability of the packaging, including closures, in terms of its strength, leakproofness and resistance to normal transport and handling, must be determined in accordance with ADR Methods 3552, 3553, 3560, 3554, 3555, 3556 and 3558, or ADR Methods for intermediate bulk containers, as appropriate, and where child-resistant closures are required, in accordance with ISO standard 8317, and be reported.

4.1.3 The resistance of the packaging material to its contents must be determined in accordance with GIFAP Monograph No 17, and be reported.

4.2 *Procedures for cleaning application equipment*

Cleaning procedures for both application equipment and protective clothing must be described in detail. The effectiveness of the cleaning procedure must be fully investigated using for example biological tests, and be reported.

4.3 *Re-entry periods, necessary waiting periods or other precautions to protect man, livestock and the environment*

The information provided must follow from and be supported by the data provided for the micro-organism(s) and that provided under Sections 7 and 8.

4.3.1 Where relevant, pre-harvest intervals, re-entry periods or withholding periods necessary to minimize the presence of residues in or on crops, plants and plant products, or in or on treated areas or spaces, with a view to protecting man or livestock, must be specified *e.g.*

- pre-harvest interval (in days) for each relevant crop;
- re-entry period (in days) for livestock, to areas to be grazed;
- re-entry period (in hours or days) for man to crops, buildings or spaces treated;
- withholding period (in days) for animal feedingstuffs;
- waiting period (in days), between application and handling treated products; or
- waiting period (in days), between last application and sowing or planting succeeding crops.

4.3.2 Where necessary, in the light of test results, information on any specific agricultural, plant health or environmental conditions under which the preparation may or may not be used, must be provided.

4.4 *Recommended methods and precautions concerning: handling, storage, transport or fire*

The recommended methods and precautions concerning handling procedures (detailed) for the storage, at both warehouse and user level of plant protection products, for their transport and in the event of fire must be provided. Where relevant, information on combustion products must be provided. The risks likely to arise and the methods and procedures to minimize the hazards arising, must be specified. Procedures to preclude or minimize the generation of waste or leftovers must be provided.

Where relevant, assessment must be conducted in accordance with ISO-TR 9122.

Where relevant, the nature and characteristics of protective clothing and equipment proposed must be reported. The data provided must be sufficient to permit an evaluation to be made of the suitability and effectiveness of protective clothing and equipment concerned under realistic conditions of use (*e.g.* field or glasshouse circumstances).

4.5 ***Measures in the case of an accident***

Whether arising during transport, storage or use, detailed procedures to be followed in the event of an emergency, must be provided and include -

- containment of spillages,
- decontamination of areas, vehicles and buildings,
- disposal of damaged packaging, adsorbents and other materials,
- protection of emergency workers and bystanders, and
- first aid measures.

4.6 ***Procedures for destruction or decontamination of the plant protection product and its packaging***

Procedures for destruction and decontamination must be developed for both small quantities (user level) and large quantities (warehouse level). The procedures must be consistent with provisions in place relating to the disposal of waste and of toxic waste. The means of disposal proposed should be without unacceptable influence on the environment and be the most cost effective and practical means of disposal feasible.

4.6.1 *Controlled incineration*

In many cases the preferred or sole means to safely dispose of plant protection products (in particular the formulants contained in them), contaminated materials, or contaminated packaging, is through controlled incineration in a licensed incinerator.

The applicant must provide detailed instructions for safe disposal of plant protection products, contaminated materials, and contaminated packaging.

4.6.2 *Others*

Other methods to dispose of plant protection products, packaging and contaminated materials, where proposed, must be fully described. Data must be provided for such methods, to establish their effectiveness and safety.

5 **Analytical methods**

Introduction

The provisions of this Section only cover analytical methods required for post-registration control and monitoring purposes.

It is desirable that plant protection products, where possible, be free of contaminants. The competent authority must make a judgement as to the acceptability of contaminants present on the basis of an assessment of the risks arising for man, animals and the environment.

The production process and finished product must be subject to continuous quality control. The quality control criteria relied upon by the applicant must be described in detail.

A justification demonstrating the validity and suitability of analytical methods used for generation of data as required in accordance with this Annex or for other purposes must be provided; where necessary separate guidance will be developed for such methods on the basis of the requirements specified for methods for post-registration control and monitoring purposes.

Descriptions of methods provided must include details of equipment, materials and conditions used. The applicability of existing CIPAC methods must be reported.

As far as practicable methods proposed must employ the simplest approach possible, involve the minimum cost, and require commonly available equipment.

For this section the following applies -

impurities	any component (including contaminating micro-organisms and/or chemical substances) other than the specified micro-organism, originating from the manufacturing process or from degradation during storage;
relevant impurities	impurities that are of concern for human or animal health and/or for the environment;
metabolites	metabolites include products resulting from degradative and biosynthetic reactions taking place within the micro-organism or other organisms used to produce the micro-organism of interest,
relevant metabolites	metabolites that are of concern for human or animal health and/or for the environment;
residues	viable micro-organisms and substances produced in significant quantities by these micro-organisms that persist after the disappearance of the micro-organisms and are of concern for human or animal health and/or the environment.

On request the following samples must be provided -

(i) samples of the preparation,

(ii) samples of the micro-organism as manufactured,

(iii) analytical standards of the pure micro-organism,

(iv) analytical standards of relevant metabolites (especially toxins) and all other components included in the residue definition, and

(vi) if available, samples of reference substances for the relevant impurities.

5.1 ***Methods for the analysis of the preparation***

Full descriptions of the methods proposed for the identification and determination of the content of the micro-organism in the preparation must be provided In the case of a preparation containing more than one micro-organism, methods capable of identifying and determining the content of each in the presence of the other must be provided.

A full description of the methods proposed to ensure that the preparation does not contain other organisms than the indicated ones and to establish its uniformity, for use in regulatory laboratories must be provided.

Details of methods proposed for the identification of any contaminating micro-organisms in the preparation must be provided.

Details of methods proposed to determine the storage stability and shelf life of the preparation must be provided.

5.2 ***Methods to determine and quantify residues***

- of the active micro-organism(s),
- of relevant metabolites (especially toxins),

on and/or in crop, in foodstuffs and feeding stuffs, in animal and human body tissues and fluids, in soil, in water (including drinking water, ground water and surface water) and in air, where relevant.

Analytical methods for amount or activity of proteinaceous products should also be included, *e.g.* by testing exponential cultures and culture supernatants in an animal cell bioassay.

6 **Efficacy data**

The requirements specified in Section 6 of Part A of Annex III also apply to plant protection products containing active substances that are micro-organisms.

7 Effects on human health

It is necessary for the assessment of toxicity of preparations including their potential for pathogenicity and infectivity, that sufficient information be available in relation to the acute toxicity, irritation and sensitisation properties of the micro-organism. All available additional information concerning the mode of toxic action and toxicological profile of the micro-organism must be submitted. Particular consideration must be given to the contribution of co-formulants to the toxicity, pathogenicity and infectivity of the preparation.

All signs of infection or pathogenicity noted in toxicity testing must be noted and be reported. Toxicity testing undertaken must include clearance studies.

In the context of the influence that impurities and other components can have on toxicological behaviour, it is essential that for each study submitted, a detailed description (specification) of the material used, be provided. Tests must be conducted using the plant protection product to be authorized. In particular, it must be clear that the micro-organism used in the preparation, and the conditions of culturing it, are the same as those for which information and data are/were provided in accordance with Part B of Annex II.

A tiered approach to the testing and evaluation of health effects associated with exposure to plant protection products containing active substances that are micro-organisms, is specified.

7.1 ***Basic acute toxicity studies***

The studies, data and information to be provided and evaluated must be sufficient to permit the identification of effects following a single exposure to the plant protection product, and in particular to establish, or indicate:

- the toxicity of the plant protection product,
- toxicity of the plant protection product relative to the micro-organism,
- the time course and characteristics of observed effects with full details of behavioural changes and possible gross pathological findings at post-mortem,
- where possible the mode of toxic action, and
- the relative hazard associated with the different routes of exposure.

While the emphasis must be on estimating the toxicity ranges involved, the information generated must also permit the plant protection product to be classified in accordance with the Regulations of 2001. The information generated through acute toxicity testing is of particular value in assessing hazards likely to arise in accident situations.

7.1.1 *Acute oral toxicity*

Circumstances in which required

An acute oral test should always be carried out unless the applicant can justify to the satisfaction of the competent authority that Regulation 9 (1) (a) of the Regulations of 2001 can be invoked.
Test guideline

The test must be carried out in accordance with EEC Method B 1 or B 1 bis.

7.1.2 *Acute inhalation toxicity*

Aim of the test

The test will provide information concerning the inhalation toxicity to rats of the plant protection product.

Circumstances in which required

The test must be carried out where the plant protection product -

- is used with fogging equipment,
- is an aerosol,
- is a powder containing a significant proportion of particles of diameter < 50 μm (> 1% on a weight basis),
- is to be applied from aircraft in cases where inhalation exposure is relevant,
- is to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 μm (> 1% on a weight basis).
- contains > 10% of a volatile component.

Test guideline

The test must be carried out in accordance with EEC Method B2.

7.1.3 *Acute percutaneous toxicity*

Circumstances in which required

An acute percutaneous toxicity test should always be carried out unless the applicant can justify to the satisfaction of the competent authority that Regulation 9 (1) (a) of the Regulations of 2001 can be invoked.

Test guideline

The test must be carried out in accordance with EEC Method B3.

7.2 ***Additional acute toxicity studies***

7.2.1 *Skin irritation*

Aim of the test

The test will provide information as to the potential for skin irritancy of the plant protection product, including the potential reversibility of the effects observed.

Circumstances in which required

The skin irritancy of the plant protection product must be determined and reported, except where the formulants are not expected to be irritant to skin and the micro-organism has been shown not to be skin irritant or where it is likely, as indicated in the test guideline, that severe skin effects can be excluded.

Test guideline

The test must be carried out in accordance with EEC Method B4.

7.2.2 *Eye irritation*

Aim of the test

The test will provide information as to the potential for eye irritation of the plant protection product, including the potential reversibility of the effects observed.

Circumstances in which required

Eye irritation tests must be conducted and reported, where the formulants are suspected to be irritating to the eye, except where the micro-organism is an eye irritant or where it is likely, as indicated in the test guideline, that severe effects on the eye may be produced.

Test guideline

The test must be carried out in accordance with EEC Method B5.

7.2.3 *Skin sensitisation*

Aim of the test

The test will provide sufficient information to assess the potential of the plant protection product to provoke skin sensitization reactions.

Circumstances in which required

The test must be carried out, where the formulants are suspected of having skin sensitising properties, except where the micro-organism(s) or formulants are known to have skin sensitising properties.

Test guideline

The tests must be carried out in accordance with EEC Method B6.

7.3 ***Data on exposure***

The risks arising for those in contact with plant protection products (operators, bystanders and workers), depend on the physical, chemical and toxicological properties of the plant protection product as well as the form of the product (undiluted/diluted), its formulation type, and on the route, degree and duration of exposure. Sufficient information and data must be generated and reported to permit an assessment to be made of the extent of exposure to the plant protection product likely to occur under the proposed conditions for its use.

Where there is particular concern regarding the possibility of dermal absorption on the basis of the information and data for the micro-organism provided in accordance with Section 5 of Part B of Annex II, or on the basis of information provided for the preparation in accordance with this Annex, further dermal absorption data may be required by the competent authority.

Results obtained through exposure monitoring conducted during production or use of the product must be submitted.

The data and information provided must also provide a basis for the selection of appropriate protective measures including personal protective equipment to be used by operators and workers and to be specified on the label.

7.4 ***Available toxicological data relating to non-active substances***

A copy of the safety data sheet prepared in accordance with the provisions of Commission Directive 91/155/EEC [64] of 5 March 1991 defining and laying down the detailed arrangements for the system of specific information relating to dangerous preparations in implementation of Article 10 of Directive 88/379/EEC [65] must be provided for each formulant.

All other available toxicological information concerning formulants must be submitted.

[64] O.J. No L76/35 22/3/1991

[65] O.J. No L187/14 16/7/1988

7.5 ***Supplementary studies for combinations of plant protection products***

Aim of the test

In certain cases it may be necessary to carry out the tests referred to in points 7.1 to 7.2.3 for a combination of plant protection products where the product label includes requirements for use of the plant protection product with other plant protection products and/or with adjuvants as a tank mix. Decisions as to the need for supplementary studies must be made on a case by case basis, taking into account the results of the acute toxicity studies of the individual plant protection products, the possibility for exposure to the combination of the products concerned and available information or practical experience with the products concerned or similar products.

7.6 ***Summary and evaluation of health effects***

A summary of data and information provided in accordance with points 7.1 through 7.5, must be provided, and include a detailed and critical assessment of those data in the context of relevant evaluative and decision making criteria and guidelines, having particular regard to the risks for man and animals that may or do arise, and the extent, quality and reliability of the data base.

8 **Residues in or on treated products, food and feed**

Introduction

(i) The requirements for individual plant protection products that follow are the same as those specified in Section 6 of Part B of Annex II. The data and information specified must be provided unless it is possible to extrapolate the residue behaviour of the plant protection product on the basis of the data and information provided for the micro-organism. Particular consideration must be given to the contribution of co-formulants to the residue behaviour of the micro-organism and its metabolites.

(ii) The information provided, taken together with that for the micro-organism, must be sufficient to permit an evaluation to be made as to the risk for man and/or animals, arising from exposure to residual traces of the micro-organism and metabolites (toxins) remaining in or on plants or plant products.

(iii) In addition, the information provided must be sufficient to:

- permit a decision to be made as to whether or not the plant protection product can be authorized,
- specify appropriate conditions or restrictions to be associated with any authorization to be granted,
- where relevant, set maximum residue levels, pre-harvest intervals to protect consumers and waiting periods to protect workers handling treated crops and products.

(iv) Experimental data on levels of exposure to residues may not be required where a justification is provided, demonstrating that the micro-organism and its metabolites do not present risks to the health of consumers in the concentrations that could occur as a consequence of authorized use. Such a justification can be based upon open literature information, practical experience and information submitted in accordance with Annex II and Annex III.

8.1 ***Persistence and likelihood of multiplication in or on crops, feedingstuffs or foodstuffs***

A quantitative estimate of the persistence/competitiveness of the micro-organism and relevant secondary metabolites (especially toxins) in or on treated crops of plant products under the environmental conditions prevailing at and after the intended use, taking into account in particular the information provided in Section 2, of Part B of Annex II must be provided.

In addition, a statement must be provided indicating the extent and basis on which it is considered that the micro-organism can (or cannot) multiply in or on plants or plant products or during processing of raw products.

8.2 ***Further information required***

Since consumers may be exposed to micro-organisms for a considerable time as a result of consumption of treated food commodities; a toxicological endpoint for risk management purposes, such as the ADI, must be established on the basis of chronic or semi-chronic studies.

8.2.1 *Non-viable residues*

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

If the micro-organism or metabolites produced by it, especially toxins, are persistent (*cf* points 2.4 and 2.5 of Part B of Annex II), full experimental residue data as provided for in Section 8 of Part A, must be provided, where the concentrations of the micro-organism and/or its toxins in or on the treated foodstuffs or feedingstuffs are expected to occur -

- in concentrations higher than under natural conditions, or
- in a different phenotypic state.

Conclusions concerning natural concentrations and elevated concentration due to treatment with the micro-organism, must be based on experimental data, and not on extrapolations or calculations made using models.

Before performing such studies, the applicant must seek the agreement of the competent authority on the type of studies to be performed.

8.2.2 *Viable residues*

If the information submitted in accordance with point 8.1, is indicative of relevant amounts of the micro-organism in or on treated products, food or feed, being persistent, possible effects on humans and/or animals must be investigated, unless it can be justified on the basis of the information and data provided in accordance with Section 5 of Part B of Annex II and Section 7, that the micro-organism and its metabolites and/or degradation products do not have harmful effects on humans in the concentrations and form that could occur as a result of authorised use.

Conclusions concerning natural concentrations and elevated concentration due to treatment with the micro-organism, must be based on experimental data, and not on extrapolations or calculations made using models.

Particular attention to the persistence of viable residues is necessary where infectivity or pathogenicity to mammals occur (*cf* points 2.3 and 2.5 and Section 5 of Part B of Annex II) and/or if any other information suggests a hazard to consumers and/or workers. In such cases, the competent authority may require submission of studies similar to those provided for in Part A of this Annex.

Before performing such studies, the applicant must seek the agreement of the competent authority on the type of studies to be performed.

8.3 ***Summary and evaluation of residue behaviour resulting from data submitted in accordance with points 8.1 and 8.2.***

9 Fate and behaviour in the environment

Introduction

(i) The requirements for individual plant protection products that follow are the same as those specified in Section 7 of Part B of Annex II. The data and information specified must be

provided unless it is possible to extrapolate the fate and behaviour of the plant protection product on the basis of the data and information provided for the micro-organism.

(ii) Information on the origin, properties, and survival of the micro-organism and its residual metabolites as well as its intended use form the basis for an assessment of environmental fate and behaviour.

Experimental data are required unless a justification is provided demonstrating that an assessment of fate and behaviour in the environment can be completed on the basis of existing information. Justifications can be based on information and data in the open literature, on practical experience and, on information provided in accordance with the requirements specified in Annex II and III. The origin and natural occurrence of the micro-organism (*cf* point 2.1.2 of Part B of Annex II) is of particular relevance in preparing such justifications.

(iii) The information provided, taken together with other relevant information, and that for the micro-organism, must be sufficient to permit an assessment of its fate and behaviour as well as that of its residual traces and toxins, where they are of significance for human health and/or the environment.

(iv) In particular, the information provided for the plant protection product, together with other relevant information, and that for the micro-organism should be sufficient -

- to decide whether, or not, the plant protection product can be authorized,
- to specify appropriate conditions or restrictions to be associated with any authorization to be granted,
- to specify the hazard symbols, the indications of danger, and relevant risk and safety phrases for the protection of the environment, which are to be included on packaging (containers),
- to predict the distribution, fate, and behaviour in the environment of the micro-organism and its metabolites as well as the time courses involved,
- to identify non-target species and populations for which hazards arise because of potential exposure, and
- to identify measures necessary to minimize contamination of the environment and impact on non-target species.

(v) Relevant metabolites (*i.e.* of concern for human health and/or the environment) formed by the test organism under relevant environmental conditions must be characterised. Where relevant metabolites are present in or produced by the micro-organism, data as specified in Section 9 of Part A of this Annex may be required, where the following conditions are met -

- the relevant metabolite is stable outside the micro-organism (*cf* point 2.8 of Part B of Annex II), and
- a toxic effect produced by the relevant metabolite occurs in the absence of the micro-organism, and
- the relevant metabolite is likely to occur in the environment in concentrations considerably higher than under natural conditions.

(vi) Available information concerning relationship to naturally occurring wild type relatives must be taken into account.

(vii) Before undertaking studies as referred to hereunder, the applicant must seek the agreement of the competent authority on the need for such studies and on their design. Information generated in accordance with other Sections of this Annex must also be taken into account.

9.1 ***Persistence and multiplication***

Information on the persistence and multiplication of the micro-organism, in all relevant environmental compartments must be provided, unless a justification has been submitted demonstrating that exposure of the particular environmental compartment to the micro-organism is unlikely to occur. Special attention must be given to -

- competitiveness under the environmental conditions prevailing at and after the intended use, and
- population dynamics in seasonally or regionally extreme climates (particularly hot summer, cold winter and rainfall) and to agricultural practices applied after intended use.

Estimates of the levels of the micro-organism occurring over time, following use of the product under the proposed conditions of use, must be provided.

9.1.1 *Soil*

Information on viability/population dynamics must be reported for several cultivated and non-cultivated soils representative of the range of soils in the various Community regions where use exists or is anticipated. The provisions on choice of soil and its collection and handling, specified in point 7.1 of Part A of Annex II, must be followed. If the test organism is to be used in association with other media (*e.g.* rockwool), this must be included in the testing regimen.

9.1.2 *Water*

Information on viability/population dynamics in natural sediment/water systems under both dark and illuminated conditions must be reported.

9.1.3 *Air*

Where there are particular concerns in relation to operator, worker or bystander exposure, information on the concentrations in air may be required.

9.2 ***Mobility***

The possible movement of the micro-organism and its degradation products into other environmental compartments must be evaluated, unless a justification is submitted demonstrating that exposure of the environmental compartments concerned to the micro-organism is unlikely to occur. Such justifications may include information concerning the intended use (*e.g.* field or greenhouse, application to soil or to crops), life cycle stages, including occurrence of vectors, persistence and the ability of the organism to colonise adjacent habitats.

Particular attention must be paid to the spread, the persistence and probable transport ranges of the micro-organism where toxicity, infectivity or pathogenicity have been reported or if any other information suggests possible hazard to humans, animals or to the environment. In such

cases the competent authority may require studies similar to specified in Part A of this Annex to be conducted and reported. Before undertaking such studies, the applicant must seek the agreement of the competent authority on the type of studies to be performed.

10 **Effects on non-target organisms**

Introduction

(i) The information provided, taken together with that for the micro-organism(s), must be sufficient to permit an assessment to be made of the impact on non-target species (flora and fauna) of the plant protection product, when used as proposed. Such impact can result from single, prolonged or repeated exposure, and can be reversible, or irreversible.

(ii) The choice of non-target organisms made for testing to identify and quantify environmental effects should reflect the identity, characteristics and properties of the micro-organism (*cf* Part B of Annex II) and information on formulants and other components of the preparation as specified in this Annex. On the basis of that information it should be possible to choose appropriate test organisms, such as organisms closely related to the target organism.

(iii) The information provided for the plant protection product, together with other relevant information, and that provided for the micro-organism, should be sufficient to -

- permit an evaluation of the short and long term risks for non-target species - populations, communities, and processes as appropriate,
- specify the hazard symbols, the indications of danger, and relevant risk and safety phrases for the protection of the environment, to be mentioned on packaging (containers), and
- permit specification of any special precautions are necessary for the protection of non-target species.

(iv) There is a need to report all potentially adverse effects found during routine ecotoxicological testing and to undertake and report such additional studies which may be necessary to investigate the probably mechanisms involved and to assess the significance of these effects.

(v) In general, much of the data concerning impact on non-target species, required for authorization of plant protection products, will have been submitted and evaluated for the inclusion of the micro-organism(s) in Annex I.

(vi) Where exposure data are necessary to facilitate decision-making concerning the need for any particular study, the data provided in accordance with the provisions of Section 9 should be relied upon.

For the estimation of the degree of exposure of particular organisms all relevant information on the plant protection product and on the micro-organism contained in the product must be taken into account. Where relevant the information specified in this Section should be used. Where it appears from available data that the plant protection product is more potent than the micro-organism, data on the effects of the plant protection product on non target organisms must be used in calculating relevant effect/exposure ratios.

(vii) In order to facilitate the assessment of the significance of test results obtained, the same strain (of recorded origin) of each relevant species should where possible be used in the various tests specified.

10.1 ***Effects on birds***

The toxicity, infectivity and pathogenicity to birds of the plant protection product must be determined and be reported, where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless a justification is submitted demonstrating that exposure of birds is unlikely to occur.

Aim of the test

Information on toxicity, infectivity and pathogenicity to birds must be reported.

10.2 ***Effects on aquatic organisms***

The toxicity, infectivity and pathogenicity to aquatic organisms of the plant protection product must be determined and be reported, where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless a justification is submitted demonstrating that exposure of aquatic organisms is unlikely to occur.

Aim of the test

Information on toxicity, infectivity and pathogenicity to aquatic organisms must be reported.

10.3 ***Effects on bees***

The toxicity, infectivity and pathogenicity to bees of the plant protection product must be determined and be reported, where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless a justification is submitted demonstrating that exposure of bees is unlikely to occur.

Aim of the test

Information on toxicity, infectivity and pathogenicity to bees must be reported.

10.4 ***Effects on arthropods other than bees***

The toxicity, infectivity and pathogenicity to arthropod species other than bees of the plant protection product must be determined and be reported, where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless a justification is submitted demonstrating that exposure of arthropod species other than bees is unlikely to occur.

Aim of the test

Information on toxicity, infectivity and pathogenicity to arthropod species other than bees must be reported.

10.5 ***Effects on earthworms***

The toxicity, infectivity and pathogenicity to earthworms of the plant protection product must be determined and be reported, where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless a justification is submitted demonstrating that exposure of earthworms is unlikely to occur.

Aim of the test

Information on toxicity, infectivity and pathogenicity to earthworms must be reported.

10.6 ***Effects on soil micro-organisms***

The effects on soil micro-organisms of the plant protection product must be determined and be reported, where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless a justification is submitted demonstrating that exposure of soil micro-organisms is unlikely to occur.

Impact on relevant non-target micro-organisms and on their predators (*e.g.* protozoa for bacterial inoculants) must be reported. Expert judgement is necessary to decide whether or not additional studies are necessary. Due consideration should be given to data and information provided in accordance with Part B of Annex II, in particular data on the specificity of the micro-organism, and expected exposure. Useful information may also be available from observations made in the course of efficacy testing. Particular attention should be given to organisms used in integrated crop management (ICM).

10.7 ***Additional studies***

Expert judgement is required to decide whether or not additional studies are necessary. Decisions made should take account available information provided in accordance with this and other Sections, in particular data and information on the specificity of the micro-organism, and the expected degree and duration of exposure. Useful information may also be available from the observations made in the course of efficacy testing.

Particular attention should be given to possible effects on naturally occurring and deliberately released organisms of importance in IPM. In particular the compatibility of the product with IPM should be taken into consideration.

Additional studies conducted might include testing on additional species or higher tier studies such as chronic, sub-lethal or reproductive studies on selected non-target organisms. Before performing such studies, the applicant must seek the agreement of the competent authority on the type of study to be performed.

11 **Summary and evaluation of environmental impact**

A summary and evaluation of all data relevant to environmental impact should be carried out in accordance with the guidance documents specified in **Fourth Schedule**. The summary and

evaluation provided should include a detailed and critical assessment of the supporting data in the context of relevant evaluative and decision making criteria and guidelines, having particular regard to the risks for the environment and non-target species that may or do arise, and the extent, quality and reliability of the data base.

The following particular issues must be addressed:

- distribution and fate in the environment, and the time courses involved;
- identification of non-target species and populations at risk, and the extent of their potential exposure;
- identification of precautions necessary to avoid or minimise contamination of the environment, and for the protection of non-target species.

12 Further information

12.1 ***Information on authorization in other countries***

12.2 ***Information on established maximum residue limits (MRLs) in other countries***

12.3 ***Proposals including justification for the classification and labelling proposed in accordance with the Regulations of 2001***

- Hazard symbol(s)
- Indication of danger
- Risk phrases
- Safety phrases

12.4 ***Proposals for risk and safety phrases in accordance with Regulation 24 (3) (h) and (i) and the proposed label***

12.5 ***Specimens of proposed packaging***

Appendix 4

Annex IV to Directive 91/414/EEC

(Annex IV to the Directive of 1991)

Pro Memoria

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Appendix 5

Annex V to Directive 91/414/EEC

(Annex V to the Directive of 1991)

Pro Memoria

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Appendix 6

Annex VI to Directive 91/414/EEC

(Annex VI to the Directive of 1991, as amended by Council Directive 97/57/EC of 22 September 1997)

UNIFORM PRINCIPLES FOR EVALUATION AND AUTHORIZATION OF PLANT PROTECTION PRODUCTS

CONTENTS

2.5 *Influence on the environment*
2.5.1 Fate and distribution in the environment
2.5.2 Impact on non-target species

2.6 *Analytical methods*

2.7 *Physical and chemical properties*

A **INTRODUCTION**

1 The principles developed in this Annex are intended to ensure that evaluations and decisions with regard to the authorization of plant protection products, provided they are chemical preparations, result in the implementation of the requirements of Article 4 (1) (b), (c), (d) and (e) of the Directive of 1991, by the competent authority, in a manner that achieves a high level of protection of human and animal health and the environment.

2 In evaluating applications and granting authorizations the competent authority shall:

(a)
- without prejudice to the provisions of subparagraph (3) (a) of Regulation 8 and paragraph (3) of Regulation 10 of the principal Regulations, ensure that the dossier supplied is in accordance with the requirements of Annex III, at the latest at the time of finalization of the evaluation for the purpose of decision-making,
- ensure that the data submitted are acceptable in terms of quantity, quality, consistency and reliability and are sufficient to permit a proper evaluation of the dossier,
- evaluate, where relevant, justifications submitted by the applicant for not supplying certain data;

(b) without prejudice, where relevant, to the provisions of subparagraphs (3) (b) and (5) (a) of Regulation 8 and paragraphs (1) and (2) of Regulation 10 of the principal Regulations, take into account the Annex II data concerning the active substance in the plant protection product, submitted for the purpose of inclusion of the active substance concerned in Annex I, and the results of the evaluation of those data; and

(c) take into consideration other relevant technical or scientific information that it possesses 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 Annex II data, 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 shall be evaluated and a decision made for the proposed use.

Taking account of justifications provided and with the benefit of any subsequent clarifications, the competent authority shall reject applications for which the data gaps are such that it is not possible to finalize 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, the competent authority shall co-operate with applicants, to resolve any questions relating to the dossier quickly, to identify at an early stage any additional studies necessary for a proper evaluation of the dossier, 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 the Regulations.

The competent authority 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 Annex III.

6 The judgements made by the competent authority during the evaluation and decision-making process shall be based on scientific principles, preferably recognized at international level (for example, by the EPPO), and be made with the benefit of the expert advice available to it.

B EVALUATION

1 General principles

1.1 Having regard to current scientific and technical knowledge, the competent authority shall evaluate the information referred to in Part A, point 2, and in particular:

(a) assess the performance in terms of efficacy and phytotoxicity of the plant protection product for each use for which authorization is sought, and

(b) identify the hazards arising, assess their significance and make a judgement as to the likely risks to humans, animals or the environment.

1.2 In accordance with the terms of Article 4 of the Directive of 1991, 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, the competent authority 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 the competent authority shall also take into account the principles of integrated control.

1.3 In the evaluation of applications submitted, the competent authority 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, the competent authority 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 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 the range of use conditions that are likely to occur, 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 the 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, and
- 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 criterion concerned shall be taken into account.

2 **Specific principles**

The competent authority 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, the competent authority 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, the competent authority 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 The competent authority shall evaluate the efficacy data on the plant protection product as provided for in Annex III 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, and
- the type of application equipment.

2.1.4 The competent authority 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; and

(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, the competent authority 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, the competent authority 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, the competent authority shall evaluate the appropriateness of the mix and of its conditions of use.

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

2.2.1 The competent authority shall evaluate the degree of adverse effects on the treated crop after use of the plant protection product according to 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 will take into consideration the following information:

(i) the efficacy data provided for in Annex III;

(ii) other relevant information on the plant protection product such as nature of the preparation, dose, method of application, number and timing of applications; and

(iii) all relevant information on the active substance as provided for in Annex II, including mode of action, vapour pressure, volatility and water solubility.

(b) This evaluation will include:

(i) the nature, frequency, level and duration of observed phytotoxic effects and the agricultural, plant health and environmental (including climatic) conditions that affect these;

(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; and

(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 debris in significant quantities after use of the plant protection product according to the proposed conditions of use, the competent authority 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 2.2.1 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 is intended to have an effect on vertebrates, the competent authority 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 it shall evaluate the time necessary to obtain the death of the animal and the conditions under which death occurs.

This evaluation will take into consideration the following information :

(i) all relevant information as provided for in Annex II and the results of the evaluation thereof, including the toxicological and metabolism studies; and

(ii) all relevant information on the plant protection product as provided for in Annex III, including toxicological studies and efficacy data.

2.4 *Impact on human or animal health*

2.4.1 *arising from the plant protection product*

2.4.1.1 The competent authority 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 Annex II 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 Annex III, including where appropriate dermal absorption studies; and

(iv) other relevant information as provided for in Annex III 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.

(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 The competent authority shall examine the 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, and
- its resistance to and compatibility with the contents.

2.4.1.3 The competent authority shall examine the nature and characteristics of the protective clothing and equipment proposed with particular reference to the following aspects -

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

2.4.1.4 The competent authority 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 Annex II and the results of the evaluation thereof, including the acceptable operator exposure level;

(ii) the toxicological studies provided for in Annex III, including where appropriate dermal absorption studies; and

(iii) other relevant information on the plant protection product as provided for in Annex III 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, and
- further activities whereby workers are exposed.

2.4.2 *arising from residues*

2.4.2.1 The competent authority shall evaluate the specific information on toxicology as provided for in Annex II 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, and
- 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, the competent authority shall examine the following information -

- data on the proposed good agricultural practice, including data on application as provided for in Annex III 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, and
- analytical methods and the residue definition.

2.4.2.3 On the basis of suitable statistical models the competent authority shall evaluate the residue levels observed in the trials reported. 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 Annex III 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 Annex II and the results of the evaluation thereof; and

(iv) the realistic possibilities of extrapolating data from one crop to another.

2.4.2.4 The competent authority shall evaluate the residue levels observed in products of animal origin, taking into consideration the information provided for in Annex III, Part A, point 8.4 and residues resulting from other uses.

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

2.4.2.6 The competent authority 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, the competent authority shall have regard to all aspects of the environment, including biota, and in particular to the following:

2.5.1.1 The competent authority shall evaluate the possibility that the plant protection product may reach the soil under the proposed conditions of use; if this possibility exists it shall estimate the rate and the route of degradation in the soil, mobility in the soil and the change in the total concentration (extractable and non-extractable [66]) 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 according to 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 Annex II 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 Annex III, including the information on distribution and dissipation in soil; and

(iv) where relevant, other authorized 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 The competent authority shall evaluate the possibility that the plant protection product may reach ground water under the proposed conditions of use; if this possibility exists, it shall estimate, using a suitable calculation model validated at Community level, the concentration of the active substance and of relevant metabolites, degradation and reaction products that could be expected in the ground water in the area of envisaged use after use of the plant protection product according to the proposed conditions of use.

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[66] 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 according to 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.

If there is not a validated Community calculation model, the competent authority shall base its evaluation on the results of studies on mobility and persistence in soil as provided for in Annexes II and III.

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 Annex II 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 Annex III, including the information on distribution and dissipation in soil and water;

(iv) where relevant, other authorized 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 and reaction products in ground water 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 The competent authority shall evaluate the possibility that the plant protection product may reach surface water under the proposed conditions of use; if this possibility exists it shall estimate, using a suitable calculation model validated at Community 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 according to the proposed conditions of use.

If there is not a validated Community calculation model, the competent authority shall base its evaluation on the results of the studies on mobility and persistence in soil and the information on run-off and drift as provided for in Annexes II and III.

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 Annex II 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 relevant information on the plant protection product as provided for in Annex III, 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 via the atmosphere;

(v) where relevant, other authorized uses of plant protection products in the area of envisaged use containing the same active substance or which give rise to the same residues; and

(vi) where relevant, data on the procedures for drinking water abstraction and treatment in the area of envisaged use.

2.5.1.4 The competent authority shall evaluate the possibility that the plant protection product may be dissipated in the air under the proposed conditions of use; if this possibility exists it 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 according to 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 Annex II 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 Annex III, including the information on distribution and dissipation in air.

2.5.1.5 The competent authority 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 the competent authority shall take into consideration toxicity to the most sensitive relevant organism used in the tests.

2.5.2.1 The competent authority 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 it shall evaluate the extent of the short-term and long-term risks to be expected for these organisms, including reproductive effects, after use of the plant protection product according to 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 Annex II and the results of the evaluation thereof;

(ii) all relevant information on the plant protection product as provided for in Annex III, including the information on effects on birds and other non-target terrestrial vertebrates; and

(iii) where relevant, other authorized 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 ratios. The toxicity/exposure ratios are defined as, respectively, the quotient of LD_{50}, LC_{50} or non-observable effect concentration (NOEC) expressed on an active substance basis and the estimated exposure expressed in mg/kg body weight.

2.5.2.2 The competent authority shall evaluate the possibility that exposure of aquatic organisms to the plant protection product may occur under the proposed conditions of use; if this possibility exists it shall evaluate the degree of short-term and long-term risks to be expected for aquatic organisms after use of the plant protection product according to the proposed conditions of use.

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

(i) the specific information relating to the effects on aquatic organisms as provided for in Annex II 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,
- K_{OC},
- 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 Annex III and in particular the effects on aquatic organisms;

(iv) where relevant, other authorized 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 ratios for fish and Daphnia. These ratios are defined as the quotient of respective acute LC_{50} or EC_{50} 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_{50} and the predicted short-term environmental concentration;

(iv) a calculation of the long-term toxicity/exposure ratios for fish and Daphnia. The long-term toxicity/exposure ratios are defined as the quotient of the NOEC levels and the predicted long-term environmental concentration;

(v) where relevant, bioconcentration in fish and possible exposure of predators of fish, including humans; and

(vi) if the plant protection product is to be applied directly to surface water, effects on surface water quality, such as pH or dissolved oxygen content.

2.5.2.3 The competent authority shall evaluate the possibility that exposure of honeybees may occur to the plant protection product under the proposed conditions of use; if this possibility exists it shall evaluate the short-term and long-term risks to be expected for honeybees after use of the plant protection product according to 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 Annex II 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 Annex III, including toxicity to honeybees; and

(iv) where relevant, other authorized 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 ratios between the maximum application rate expressed in grammes of active substance per hectare and the contact and oral LD_{50} 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; and

(ii) where relevant, effects on honeybee larvae, honeybee behaviour, colony survival and development after use of the plant protection product according to the proposed conditions of use.

2.5.2.4 The competent authority 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 it shall assess expected lethal and sub lethal effects on these organisms and the reduction in their activity after use of the plant protection product according to 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 Annex II 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 Annex III such as -

- effects on beneficial arthropods other than bees,
- toxicity to honeybees,
- available data from biological primary screening,
- maximum application rate,
- maximum number and timetable of applications;

(iv) where relevant, other authorized 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 The competent authority 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 it shall evaluate the degree of short-term and long-term risks to be expected to these organisms after use of the plant protection product according to 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 Annex II and the results of the evaluation thereof;

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

- solubility in water,
- octanol/water partition coefficient,
- Kd for adsorption,
- vapour pressure,
- hydrolysis rate in relation to pH and identity of breakdown products,
- photodegradation rate and identity of breakdown products,
- DT_{50} and DT_{90} for degradation in the soil;

(iii) all relevant information on the plant protection product as provided for in Annex III, including the effects on earthworms and other non-target soil macro-organisms; and

(iv) where relevant, other authorized 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) lethal and sub lethal effects;

(ii) 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); and

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

2.5.2.6 The competent authority shall, where the evaluation carried out under Part B, 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 impact on microbial activity such as impact on nitrogen and carbon mineralization processes in the soil after use of the plant protection product according to 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 on non-target soil micro-organisms as provided for in Annex II and the results of the evaluation thereof;

(ii) all relevant information on the plant protection product as provided for in Annex III, including the effects on non-target soil micro-organisms;

(iii) where relevant, other authorized uses of plant protection products in the area of proposed use, containing the same active substance or which give rise to the same residues; and

(iv) all available information from biological primary screening.

2.6 *Analytical methods*

The competent authority 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) data on analytical methods as provided for in Annex II and the results of the evaluation thereof;

(ii) data on analytical methods as provided for in Annex III, in particular -

- the specificity and linearity of the proposed methods,
- the importance of interferences,
- the precision of the proposed methods (intra-laboratory repeatability and inter-laboratory reproducibility); and

(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 authorized uses of the plant protection product and which are of toxicological, ecotoxicological or environmental significance.

This evaluation shall take into consideration the following information:

(i) data on analytical methods as provided for in Annex II and the results of the evaluation thereof;

(ii) data on analytical methods as provided for in Annex III, in particular -

- the specificity of the proposed methods,
- the precision of the proposed methods (intra-laboratory repeatability and inter-laboratory reproducibility),
- the recovery rate of the proposed methods at appropriate concentrations;

(iii) the limit of detection of the proposed methods; and

(iv) the limit of determination of the proposed methods.

2.7 *Physical and chemical properties*

2.7.1 The competent authority shall evaluate the actual content of the active substance in the plant protection product and its stability during storage.

2.7.2 The competent authority shall evaluate the physical and chemical properties of the plant protection product and in particular -

- where a suitable FAO 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 specifications for plant protection products".

This evaluation shall take into consideration the following information:

(i) data on the physical and chemical properties of the active substance as provided for in Annex II and the results of the evaluation thereof; and

(ii) data on the physical and chemical properties of the plant protection product as provided for in Annex III.

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 shall be evaluated.

C **DECISION-MAKING**

1 ***General principles***

1 Where appropriate, the competent authority shall impose conditions or restrictions on authorizations that it grants. The nature and severity of these measures shall be selected on the basis of, and be appropriate to, the nature and extent of the expected advantages and the risks likely to arise.

2 The competent authority shall ensure that, where necessary, decisions taken with respect to the granting of authorizations take account of the agricultural, plant health and environmental (including climatic) conditions in the areas of envisaged use. Such considerations may result in specific conditions and restrictions on use, and, where necessary, may result in authorization being granted for some but not other areas within the territory of the State.

3 The competent authority shall ensure that the authorized 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 authorized amounts shall be differentiated according to, and be appropriate to the agricultural, plant health and environmental (including climatic) conditions in the various areas for which an authorization is granted. However, the rates and the number of applications shall not give rise to undesirable effects such as the development of resistance.

4 The competent authority shall ensure that decisions taken respect the principles of integrated control if the product is intended to be used in conditions where these principles are relied on.

5 Since the evaluation is to be based on data concerning a limited number of representative species, the competent authority shall ensure that use of plant protection products does not have any long-term repercussions for the abundance and diversity of non-target species.

6 Before issuing an authorization, the competent authority shall ensure that the label of the product -

- fulfils the requirements of Regulation 24 of the principal Regulations,
- also contains the information on protection of users required by Community 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, 2, 3, 4 and 5 above.

The authorization shall mention the particulars specified in subparagraphs (2) (g), (ii), (iii), and (iv) and subparagraphs (i) and (j) of Regulation 24 of the principal Regulations.

7 Before issuing authorizations, the competent authority shall:

(a) ensure that the proposed packaging is in accordance with the provisions of Regulation 23 of the principal Regulations; and

(b) ensure that -

- the procedures for destruction of the plant protection product,
- the procedures for neutralization of the adverse effects of the product if it is accidentally dispersed,
- the procedures for the decontamination and destruction of the packaging,

are in accordance with the relevant regulatory provisions.

8 No authorization 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 Part C, points 2.1, 2.2, 2.3 or 2.7, are not fully satisfied, authorizations 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 shall be mentioned on the label, and non-compliance with the requirements referred to in point 2.7 shall 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 minimize the risk of development of resistance,
- 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 Part C, point 2.6, are not fully satisfied because of limitations in current analytical science and technology, authorization 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 the criteria referred to above. The authorization 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 Part C, point 2.6, has only been verified in two laboratories, an authorization shall be granted for one year to permit the applicant to demonstrate the reproducibility of those methods in accordance with agreed criteria.

9 Where an authorization has been granted according to the requirements provided for in this Annex, the competent authority may, by virtue of subparagraph (6) (b) of Regulation 19 of the principal Regulations:

(a) define, where possible, preferably in close co-operation with the applicant, measures to improve the performance of the plant protection product, and/or

(b) define, where possible, in close co-operation with the applicant, measures to reduce further the exposure that could occur during and after use of the plant protection product.

The competent authority 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 authorization shall be granted for those uses.

2.1.2 The level, consistency and duration of control or protection or other intended effects shall be similar to those resulting from the use of suitable reference products. If no suitable reference product exists, the plant protection product shall 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.

2.1.3 Where relevant, yield response when the product is used and reduction of loss in storage shall 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 shall 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 shall be valid for all areas of the territory of the State, and shall 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 shall 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 other specified plant protection products or adjuvants as a tank mix, the competent authority shall not accept the recommendations unless they are justified.

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

2.2.1 There shall 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 shall 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 shall 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.

2.2.4 There shall 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 shall 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.

2.2.6 There shall 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 shall comply with the principles referred to in points 2.2.1 to 2.2.6.

2.2.8 The proposed instructions for cleaning the application equipment shall 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 that could subsequently cause damage.

2.3 *Impact on vertebrates to be controlled*

An authorization 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 *arising from the plant protection product*

2.4.1.1 No authorization 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 acceptable operator exposure level (AOEL).

Moreover, the conditions of the authorization 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 80/1107/EEC of 27 November 1980 on the protection of workers from the risks related to exposure to chemical, physical and biological agents at work [67] and Council Directive 90/394/EEC of 28 June 1990 on the protection of workers from the risks related to exposure to carcinogens at work [68].

2.4.1.2 Where the proposed conditions of use require use of items of protective clothing and equipment, no authorization shall be granted unless those items are effective and in accordance with the relevant Community 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, shall 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 that are classified as very toxic shall not be authorized for use by non-professional users.

2.4.1.4 Waiting and re-entry safety periods or other precautions shall 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 provisions referred to in point 2.4.1.1.

2.4.1.5 Waiting and re-entry safety periods or other precautions shall 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 shall be realistic; if necessary special precautionary measures shall be prescribed.

2.4.2 *arising from residues*

2.4.2.1 Authorizations shall 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.

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[67] O.J. No. L327/8 3/12/1980. Directive as last amended by Directive 88/642/EEC O.J. No. L356/74 24/12/1988

[68] O.J. No. L196/1 26/7/1990. Directive as last amended by Directive 97/42/EC O.J. No. L179/4 8/7/1997

2.4.2.2. Where no Community maximum residue limit (MRL) [69] or provisional MRL (at national or at Community level) exists, the competent authority shall establish a provisional MRL in accordance with subparagraph (1) (c) of Regulation 13, subparagraph (2) (b) of Regulation 15 or subparagraph (3) (b) of Regulation 18 of the principal Regulations; conclusions as to the levels fixed shall be valid for all circumstances which could influence the residue levels in the crop such as timing of application, application rate and frequency or manner of use.

2.4.2.3 Where the new circumstances under which the plant protection product is to be used do not correspond to those under which a provisional MRL (at national or at Community level) was established previously, the competent authority shall not grant an authorization for the plant protection product unless the applicant can provide evidence that the recommended use will not result in the MRL being exceeded, or unless a new provisional MRL has been established by the competent authority, or by the Commission in accordance with Article 4(1)(f) of the Directive of 1991.

2.4.2.4 Where a Community MRL exists the competent authority shall not grant an authorization for the plant protection product unless the applicant can provide evidence that the recommended use will not result in the MRL being exceeded, or unless a new Community MRL has been established in accordance with the procedures provided for in the relevant Community legislation.

2.4.2.5 In the cases referred to in points 2.4.2.2 and 2.4.2.3, each application for an authorization shall be accompanied by a risk assessment, taking into account worst-case potential exposure of consumers in the territory of the State, on the basis of good agricultural practice.

Taking into account all registered uses, the proposed use shall not be authorized if the best possible estimate of dietary exposure exceeds the acceptable daily intake (ADI).

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

2.4.2.7 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.

[69] A Community MRL means an MRL established pursuant to Council Directive 76/895/EEC of 23 November 1976 on the fixing of maximum levels for pesticide residues in or on fruit or vegetables (O.J. No. L340/26 9/12/1976), Council Directive 86/362/EEC of 24 July 1986 on the fixing of maximum levels for pesticide residues in or on cereals (O.J. No. L221/37 7/8/1986), Council Directive 86/363/EEC of 24 July 1986 on the fixing of maximum levels for pesticide residues in or on foodstuffs of animal origin (O.J. No. L221/43 7/8/1986), Council Regulation (EEC) No 2377/90 of 26 June 1990 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin (O.J. No. L224/1 18/8/1990), Council Directive 90/642/EEC of 27 November 1990 on the fixing of maximum levels for pesticide residues in or on certain products of plant origin, including fruit and vegetables (O.J. No. L350/71 14/12/1990), or Council Directive 91/132/EEC of 4 March 1991 amending Directive 74/63/EEC on undesirable substances and products in feedingstuffs (O.J. No. L66/16 13/3/1991).

2.5 *Influence on the environment*

2.5.1 *Fate and distribution in the environment*

2.5.1.1 No authorization 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 one year (*i.e.* DT_{90} > 1 year and DT_{50} > 3 months), or
- during laboratory tests, form non-extractable residues in amounts exceeding 70 % of the initial dose after 100 days with a mineralization 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 authorization shall be granted if the concentration of the active substance or of relevant metabolites, degradation or reaction products in ground water, 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:

(i) the maximum permissible concentration laid down by Council Directive 80/778/EEC of 15 July 1980 [70] relating to the quality of water intended for human consumption; or

(ii) the maximum concentration laid down by the Commission when including the active substance in Annex I, 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 included in Annex I;

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

2.5.1.3 No authorization 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, the values fixed by Council Directive 75/440/EEC of 16 June 1975 [71] concerning the quality required of surface water intended for the abstraction of drinking water in the Member States, or
- has an impact deemed unacceptable on non-target species, including animals, according to 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, shall be such that the likelihood of accidental contamination of surface water is reduced to a minimum.

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[70] O.J. No. L229/11 30/8/1980

[71] O.J. No. L194/34 25/7/1975

2.5.1.4 No authorization 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 Part C, 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 authorization 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_{50} 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 according to 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 according to the proposed conditions of use.

2.5.2.2 Where there is a possibility of aquatic organisms being exposed, no authorization 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 1000 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 according to the proposed conditions of use.

2.5.2.3 Where there is a possibility of honeybees being exposed, no authorization 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 according to the proposed conditions of use.

2.5.2.4 Where there is a possibility of beneficial arthropods other than honeybees being exposed, no authorization shall be granted if more than 30 % of the test-organisms are affected in lethal or sub lethal 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 according to 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 authorization 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 that under field conditions earthworm populations are not at risk after use of the plant protection product according to the proposed conditions of use.

2.5.2.6 Where there is a possibility of non-target soil micro-organisms being exposed, no authorization shall be granted if the nitrogen or carbon mineralization 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 according to the proposed conditions of use, taking account of the ability of micro-organisms to multiply.

2.6 *Analytical methods*

The methods proposed shall reflect the state of the art. The following criteria shall 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 shall be suitable for the determination and identification of 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 shall be suitable for the determination and confirmation of residues of toxicological, ecotoxicological or environmental significance;

(ii) mean recovery rates should be between 70 % and 110 % with a relative standard deviation of $\leq$ 20 %;

(iii) repeatability shall be less than the following values for residues in foodstuffs:

Residue level mg/kg	*Difference mg/kg*	*Difference in %*
001	0.005	50
0.1	0.025	25
1	0.125	12.5
>1		12.5

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

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

Residue level mg/kg	*Difference mg/kg*	*Difference 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 shall satisfy the following criteria :

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

MRL (mg/kg)	*limit of determination (mg/kg)*
> 0.5	0.1
0.5 – 0.05	0.1 – 0.02
< 0.05	MRL x 0.5

2.7 *Physical and chemical properties*

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

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

(a) C*hemical properties*

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

Declared content in g/kg or g/l at 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 shall fulfil the physical criteria (including storage stability) specified for the relevant formulation type in the "Manual on the development and use of FAO 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 shall be physically and chemically compatible in the tank mix.

Appendix 7

(Annex IV to the Directive of 1999, supplemented by the technical specifications comprising Annex IX to Directive of 1967 as amended by the Directive of 1992 and adapted by Commission Directives 91/410/EEC and 2000/32/EC)

PROVISIONS RELATING TO CHILD-PROOF FASTENINGS

PART A

Containers to be fitted with child-resistant fastenings

1. Containers of whatever capacity, containing preparations offered or sold to the general public and labelled as very toxic, toxic or corrosive in accordance with the provisions of the Regulations of 2001, are to fitted with child-resistant fastenings.

2. Containers of whatever capacity containing preparations presenting an aspiration hazard (Xn, R65), with the exception of preparations placed on the market in the form of aerosols or in a container fitted with a sealed spray attachment.

3. Containers of whatever capacity, having at least one of the substances listed in the following table, present in a concentration equal to or greater than the maximum individual concentration specified,

No	Identification of the substance			Concentration limit
	CAS-Reg No	Name	Einecs No	
1	67-56-1	Methanol	2006596	≥ 3 %
2	75-09-2	Dichloromethane	2008389	≥ 1 %

which are offered or sold to the general public are to be fitted with child-resistant fastenings.

Reclosable packages Child-proof fastenings used on reclosable packages shall comply with ISO Standard 8317 (1 July 1989 edition) relating to “Child-resistant packages - Requirements and methods of testing for reclosable packages” adopted by the International Standard Organisation (ISO).

Non-reclosable packages Child-proof fastenings used on non-reclosable packages shall comply with CEN standard EN 862 (March 1997 edition) relating to "Packaging - Child-resistant packaging - Requirements and testing procedures for non-reclosable packages for non-pharmaceutical products" adopted by the European Committee for Standardisation (CEN).

Notes 1 Evidence of conformity with the above standard may be certified only by laboratories that conform to European Standards Series EN 45 000.

2 Specific cases

If it seems obvious that packaging is sufficiently safe for children because they cannot get access to the contents without the help of a tool, the test doesn't need to be performed.

In all other cases and when there are sufficient grounds for doubting the security of the closure for a child, the competent authority may ask the person responsible for putting the product on the market to give it a certificate from a laboratory which conforms with European Standards Series EN 45 000, stating that either:

- the type of closure is such that it is not necessary to test to the ISO and CEN standards referred to above, or
- the closure has been tested and has been found to conform to the standards referred to above.

PART B

Provisions relating to tactile warnings

Containers of whatever capacity, containing preparations offered or sold to the general public and labelled as very toxic, toxic, corrosive, harmful, extremely flammable or highly flammable in accordance with the Regulation of 2001, are to carry a tactile warning of danger.

This provision does not apply to aerosols classified and labelled only as extremely flammable or highly flammable.

The technical specifications for tactile warnings devices shall conform with EN ISO standard 11683 (1997 edition) relating to “Packaging - Tactile warning of danger – Requirements”

Appendix 8

(Annex V of the Directive of 1999 as adapted by Commission Directive 2001/60/EC)

SPECIAL PROVISIONS FOR LABELLING CERTAIN PREPARATIONS

A **For preparations classified as dangerous in accordance with Regulations of 8, 9 and 10 or the Regulations of 2001**

1 *Preparations sold to the general public*

1.1 The labels on packages containing such preparations, in addition to the specific safety advice, must bear relevant safety advice S1, S2, S45 or S46 in accordance with the criteria laid down in Annex VI to the Regulations of 2001.

1.2 When such preparations are classified as very toxic (T+), toxic (T) or corrosive (C) and where it is physically impossible to give such information on the package itself, packages containing such preparations must be accompanied by precise and easily understandable instructions for use including, where appropriate, instructions for the destruction of the empty package.

2 *Preparations intended for use by spraying*

The package label containing such preparations must compulsorily bear the safety advice S23 accompanied by safety advice S38 or S51 assigned in accordance with the criteria laid down in Annex VI.

3 *Preparations containing a substance assigned phrase R33: Danger of cumulative effects*

When a preparation contains at least one substance assigned the phrase R33, the label of the preparation must carry the phrase R33, when the concentration of the substance in the preparation is equal to or higher than 1 %, unless different values are set in Annex I to the Directive of 1967.

4 *Preparations containing a substance assigned phrase R64: May cause harm to breastfed babies*

When a preparation contains at least one substance assigned phrase R64, the label of the preparation must carry the phrase R64, when the concentration of this substance present in the preparation is equal to or higher than 1 %, unless different values are set in Annex I to the Directive of 1967.

B **For preparations irrespective of their classification in accordance with Regulations 8, 9 and 10 of the Regulations of 2001**

1 *Preparations containing lead*

1.1 Paint and varnishes

Labels of packages of paints and varnishes containing lead in quantities exceeding 0.15% (expressed as weight of metal) of the total weight of the preparation, determined in accordance with 1S0 standard 6503/1984, must show the following particulars:

"Contains lead. Should not be used on surfaces liable to be chewed or sucked by children".

In the case of packages the contents of which are less than 125 ml, the particulars may be as follows:

"Warning! Contains lead.".

2 *Preparations containing cyanoacrylates*

2.1 Adhesives

The immediate packaging of adhesives based on cyanoacrylate must bear the following inscriptions:

"Cyanoacrylate

Danger

Bonds skin and eyes in seconds

Keep out of the reach of children".

Appropriate advice on safety must accompany the package.

3 *Preparations containing isocyanates*

The package labels of preparations containing isocyanates (as monomers, oligomers, prepolymers, *etc*., or as mixtures thereof) must bear the following inscriptions:

"Contains isocyanates

See information supplied by the manufacturer".

4 *Preparations containing epoxy constituents with an average molecular weight ≤ 700*

The package labels of preparations containing epoxy constituents with an average molecular weight ≤ 700 must bear the following inscriptions:

"Contains epoxy constituents

See information supplied by the manufacturer".

5 *Preparations sold to the general public, which contain active chlorine*

The packaging of preparations containing more than 1 % of active chlorine must bear the following particular inscriptions:

"Warning! Do not use together with other products. May release dangerous gases (chlorine)".

6 *Preparations containing cadmium (alloys) and intended to be used for brazing or soldering*

The packaging of the above mentioned preparations must bear the following inscription printed in clearly legible and indelible characters:

"Warning! Contains cadmium

Dangerous fumes are formed during use

See information supplied by the manufacturer

Comply with the safety instructions".

7 *Preparations available as aerosols*

Without prejudice to the provisions of theses Regulations, preparations available as aerosols are also subject to the labelling provisions specified in accordance with points 2.2 and 2.3 of the Annex to Directive 75/324/EEC [72].

8 *Preparations containing substances not yet tested completely*

Where a preparation contains at least one substance that, in accordance with Article 13.3 of the Directive of 1967, bears the inscription "Warning - substance not yet tested completely", the label of the preparation must bear the inscription "Caution - this preparation contains a substance not yet fully tested" if the substance is present in a concentration ≥ 1 %.

[72] O.J. No. L147/40 9/6/1975

9 *Preparations not classified as sensitising but containing at least one sensitising substance*

The packaging of preparations containing at least one substance classified as sensitising and present in a concentration equal to or greater than 0.1 % or in a concentration equal to or greater than that specified under a specific note for the substance in Annex I to the Directive of 1967, must bear the inscription:

"Contains (name of sensitising substance). May produce an allergic reaction".

10 *Liquid preparations containing halogenated hydrocarbons*

For liquid preparations that show no flashpoint or a flashpoint higher than 55 °C and contain a halogenated hydrocarbon and more than 5 % flammable or highly flammable substances, the packaging must bear the following inscription as appropriate:

"Can become highly flammable in use" or "'Can become flammable in use".

11 *Preparations containing a substance assigned the phrase R67: vapours may cause drowsiness and dizziness*

The packaging of preparations containing one or more substances assigned the phrase R47, must bear the wording of the phrase as set out in Annex X, when the total concentration of these substances in the preparation is equal to or higher than 15 %, unless:

- the preparation is already assigned the phrases R20, R23, R26, R68/20, R39/23 or R39/26, or
- the preparation is in a package not exceeding 125 millilitres.

12 *Cements and cement preparations*

The packaging of cements and cement preparations containing more than 0.0002 % soluble chromium (VI) on a dry weight basis must bear the inscription:

"Contains chromium (VI). May produce an allergic reaction"

unless the preparation is already classified as a sensitizer and assigned the phrase R43.

C **For preparations not classified in accordance with the provisions of Regulations 8, 9 and 10 of the Regulations of 2001 but containing at least one dangerous substance**

1 *Preparations not intended for the general public*

The label on the packaging of the preparations referred to in Regulation 23 must bear the following inscription:

"Safety data sheet available for professional user on request".

Appendix 9

(Annex II to the Directive of 1967 as amended by the Directive of 1992 and adapted by Commission Directive No.2001/59/EC)

SYMBOLS AND INDICATIONS

Note: The letters E, O, F, F+, T, T+, C, Xn, Xi and N do not form part of the symbol.

E

Explosive

O

Oxidizing

F

Highly flammable

F+

Extremely flammable

T

Toxic

T+

Very Toxic

C

Corrosive

Xn

Harmful

Xi

Irritant

N

Dangerous for the environment

Appendix 10

(Annex III to the Directive of 1967 as amended by the Directive of 1992 and adapted by Commission Directive 2001/59/EC)

NATURE OF SPECIAL RISKS

R1	Explosive when dry
R2	Risk of explosion by shock, friction, fire or other sources of ignition
R3	Extreme risk of explosion by shock, friction, fire or other sources of ignition
R4	Forms very sensitive explosive metallic compounds
R5	Heating may cause an explosion
R6	Explosive with or without contact with air
R7	May cause fire
R8	Contact with combustible material may cause fire
R9	Explosive when mixed with combustible material
R10	Flammable
R11	Highly flammable
R12	Extremely flammable
R14	Reacts violently with water
R15	Contact with water liberates extremely flammable gases
R16	Explosive when mixed with oxidising substances
R17	Spontaneously flammable in air
R18	In use, may form flammable/explosive vapour-air mixture
R19	May form explosive peroxides
R20	Harmful by inhalation

R21	Harmful in contact with skin
R22	Harmful if swallowed
R23	Toxic by inhalation
R24	Toxic in contact with skin
R25	Toxic if swallowed
R26	Very toxic by inhalation
R27	Very toxic in contact with skin
R28	Very toxic if swallowed
R29	Contact with water liberates toxic gas
R30	Can become highly flammable in use
R31	Contact with acids liberates toxic gas
R32	Contact with acids liberates very toxic gas
R33	Danger of cumulative effects
R34	Causes burns
R35	Causes severe burns
R36	Irritating to eyes
R37	Irritating to respiratory system
R38	Irritating to skin
R39	Danger of very serious irreversible effects
R40	Limited evidence of a carcinogenic effect
R41	Risk of serious damage to eyes
R42	May cause sensitisation by inhalation
R43	May cause sensitisation by skin contact
R44	Risk of explosion if heated under confinement
R45	May cause cancer
R46	May cause heritable genetic damage
R48	Danger of serious damage to health by prolonged exposure

R49	May cause cancer by inhalation
R50	Very toxic to aquatic organisms
R51	Toxic to aquatic organisms
R52	Harmful to aquatic organisms
R53	May cause long-term adverse effects in the aquatic environment
R54	Toxic to flora
R55	Toxic to fauna
R56	Toxic to soil organisms
R57	Toxic to bees
R58	May cause long-term adverse effects in the environment
R59	Dangerous for the ozone layer
R60	May impair fertility
R61	May cause harm to the unborn child
R62	Possible risk of impaired fertility
R63	Possible risk of harm to the unborn child
R64	May cause harm to breastfed babies
R65	Harmful: May cause lung damage if swallowed
R66	Repeated exposure may cause skin dryness or cracking
R67	Vapours may cause drowsiness and dizziness
R68	Possible risk of irreversible effects

Combination of R-Phrases

R14/15	Reacts violently with water, liberating extremely flammable gases
R15/29	Contact with water liberates toxic, extremely flammable gas
R20/21	Harmful by inhalation and in contact with skin
R20/22	Harmful by inhalation and if swallowed
R20/21/22	Harmful by inhalation, in contact with skin and if swallowed

R21/22	Harmful in contact with skin and if swallowed
R23/24	Toxic by inhalation and in contact with skin
R23/25	Toxic by inhalation and if swallowed
R23/24/25	Toxic by inhalation, in contact with skin and if swallowed
R24/25	Toxic in contact with skin and if swallowed
R26/27	Very toxic by inhalation and in contact with skin
R26/28	Very toxic by inhalation and if swallowed
R26/27/28	Very toxic by inhalation, in contact with skin and if swallowed
R27/28	Very toxic in contact with skin and if swallowed
R36/37	Irritating to eyes and respiratory system
R36/38	Irritating to eyes and skin
R36/37/38	Irritating to eyes, respiratory system and skin
R37/38	Irritating to respiratory system and skin
R39/23	Toxic: danger of very serious irreversible effects through inhalation
R39/24	Toxic: danger of very serious irreversible effects in contact with skin
R39/25	Toxic: danger of very serious irreversible effects if swallowed
R39/23/24	Toxic: danger of very serious irreversible effects through inhalation and in contact with skin
R39/23/25	Toxic: danger of very serious irreversible effects through inhalation and if swallowed
R39/24/25	Toxic: danger of very serious irreversible effects in contact with skin and if swallowed
R39/23/24/25	Toxic: danger of very serious irreversible effects through inhalation, in contact with skin and if swallowed
R39/26	Very toxic: danger of very serious irreversible effects through inhalation
R39/27	Very toxic: danger of very serious irreversible effects in contact with skin
R39/28	Very toxic: danger of very serious irreversible effects if swallowed
R39/26/27	Very toxic: danger of very serious irreversible effects through inhalation and in contact with skin
R39/26/28	Very toxic: danger of very serious irreversible effects through inhalation and if swallowed

R39/27/28	Very toxic: danger of very serious irreversible effects in contact with skin and if swallowed
R39/26/27/28	Very toxic: danger of very serious irreversible effects through inhalation, in contact with skin and if swallowed
R42/43	May cause sensitisation by inhalation and skin contact
R48/20	Harmful: danger of serious damage to health by prolonged exposure through inhalation
R48/21	Harmful: danger of serious damage to health by prolonged exposure in contact with skin
R48/22	Harmful: danger of serious damage to health by prolonged exposure if swallowed
R48/20/21	Harmful: danger of serious damage to health by prolonged exposure through inhalation and in contact with skin
R48/20/22	Harmful: danger of serious damage to health by prolonged exposure through inhalation and if swallowed
R48/21/22	Harmful: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed
R48/20/21/22	Harmful: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed
R48/23	Toxic: danger of serious damage to health by prolonged exposure through inhalation
R48/24	Toxic: danger of serious damage to health by prolonged exposure in contact with skin
R48/25	Toxic: danger of serious damage to health by prolonged exposure if swallowed
R48/23/24	Toxic: danger of serious damage to health by prolonged exposure through inhalation and in contact with skin
R48/23/25	Toxic: danger of serious damage to health by prolonged exposure through inhalation and if swallowed
R48/24/25	Toxic: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed
R48/23/24/25	Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed
R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
R51/53	Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
R52/53	Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

R68/20	Harmful: possible risk of irreversible effects through inhalation
R68/21	Harmful: possible risk of irreversible effects in contact with skin
R68/22	Harmful: possible risk of irreversible effects if swallowed
R68/20/21	Harmful: possible risk of irreversible effects through inhalation and in contact with skin
R68/20/22	Harmful: possible risk of irreversible effects through inhalation and if swallowed
R68/21/22	Harmful: possible risk of irreversible effects in contact with skin and if swallowed
R68/20/21/22	Harmful: possible risk of irreversible effects through inhalation, in contact with skin and if swallowed

_____

Appendix 11

(Annex IV to the Directive of 1967 as amended by the Directive of 1992 and adapted by Commission Directive 2001/59/EEC)

SAFETY ADVICE (PHRASES)

S1	Keep locked up
S2	Keep out of the reach of children
S3	Keep in a cool place
S4	Keep away from living quarters
S5	Keep contents under ...(*appropriate liquid to be proposed by the manufacturer*)
S6	Keep under ... (*inert gas to be proposed by the manufacturer*)
S7	Keep container tightly closed
S8	Keep container dry
S9	Keep container in a well-ventilated place
S12	Do not keep the container sealed
S13	Keep away from food, drink and animal feeding stuffs
S14	Keep away from .... (*incompatible materials to be indicated by the manufacturer*)
S15	Keep away from heat
S16	Keep away from sources of ignition - No smoking
S17	Keep away from combustible material
S18	Handle and open container with care
S20	When using do not eat or drink
S21	When using do not smoke
S22	Do not breathe dust

S23 Do not breathe gas/fumes/vapour/spray (*appropriate wording to be proposed by the manufacturer*)

S24 Avoid contact with skin

S25 Avoid contact with eyes

S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice

S27 Take off immediately all contaminated clothing

S28 After contact with skin, wash immediately with plenty of ... (*to be proposed by the manufacturer*)

S29 Do not empty into drains

S30 Never add water to this product

S33 Take precautionary measures against static discharges

S35 This material and its container must be disposed of in a safe way

S36 Wear suitable protective clothing

S37 Wear suitable gloves

S38 In case of insufficient ventilation, wear suitable respiratory equipment

S39 Wear eye/face protection

S40 To clean the floor and all objects contaminated by this material, use ... (*to be proposed by the manufacturer*)

S41 In case of fire and/or explosion do not breathe fumes

S42 During fumigation/spraying wear suitable respiratory equipment (*appropriate wording to be proposed by the manufacturer*)

S43 In case of fire, use ... (*indicate in the space the precise type of fire-fighting equipment. If water increases risk, add* - Never use water)

S45 In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)

S46 If swallowed, seek medical advice immediately and show this container or label

S47 Keep at temperature not exceeding ... °C (*to be proposed by the manufacturer*)

S48 Keep wetted with ... (*appropriate material to be proposed by the manufacturer*)

S49	Keep only in the original container
S50	Do not mix with ... (*to be proposed by the manufacturer*)
S51	Use only in well ventilated areas
S52	Not recommended for interior use on large surface areas
S53	Avoid exposure - obtain special instructions before use
S56	Dispose of this material and its container to hazardous or special waste collection point
S57	Use appropriate containment to avoid environmental contamination
S59	Refer to manufacturer/supplier for information on recovery/recycling
S60	This material and its container must be disposed of as hazardous waste
S61	Avoid release to the environment. Refer to special instructions/Safety data sheets
S62	If swallowed, do not induce vomiting: seek medical advice immediately and show this container or label
S63	In case of accident by inhalation: remove casualty to fresh air and keep at rest
S64	If swallowed, rinse mouth with water (only if the person is conscious)

Combination of S-Phrases

S1/2	Keep locked up and out of the reach of children
S3/7	Keep container tightly closed in a cool place
S3/9/14	Keep in a cool, well ventilated place away from ..... (*incompatible materials to be indicated by the manufacturer*)
S3/9/14/49	Keep only in the original container in a cool, well ventilated place away from ..... (*incompatible materials to be indicated by the manufacturer*)
S3/9/49	Keep only in the original container in a cool, well ventilated place
S3/14	Keep in a cool place away from ..... (*incompatible materials to be indicated by the manufacturer*)
S7/8	Keep container tightly closed and dry
S7/9	Keep container tightly closed and in a well ventilated place

S7/47 Keep container tightly closed and at a temperature not exceeding ..... °C (*to be proposed by the manufacturer*)

S20/21 When using do not eat, drink or smoke

S24/25 Avoid contact with skin and eyes

S27/28 After contact with skin, take off immediately all contaminated clothing and wash immediately with plenty of ….. (*to be specified by the manufacturer*)

S29/35 Do not empty into drains, dispose of this material and its container in a safe way

S29/56 Do not empty into drains, dispose of this material and its container to hazardous or special waste collection point

S36/37 Wear suitable protective clothing and gloves

S36/37/39 Wear suitable protective clothing, gloves and eye/face protection

S36/39 Wear suitable protective clothing and eye/face protection

S37/39 Wear suitable gloves and eye/face protection

S47/49 Keep only in the original container at temperature not exceeding .....ºC (*to be proposed by the manufacturer*)

Appendix 12

ADDITIONAL SAFETY ADVICE

FS 1 Store / keep in original container, tightly closed, in a safe place / under lock and key / away from damp / sources of heat.

FS 2 Store / keep / apply / away from / install out of reach of pets / birds / bees / fish / (young) children and animals.

or

Keep / use / suspend only in positions inaccessible to children and pets / animals.

FS 3 Store unused sachets / mats / coils in a safe place. Do not store half-used sachets / mats / coils.

FS 4 Not to be used on food crops.

FS 5 For use only on (crop / foodstuff / surface / situation) for control of (process).

FS 6 To be used only by (professional) operators (instructed / or trained / in the use of chemical / product / type of product / and familiar with the precautionary measures to be observed).

FS 7 Do not spray / apply directly to livestock / poultry / pets /pets bedding / food / food crops / skin / children's clothing **.**

FS 8 Do not apply to clothing / fabric / bedding / hard / soft furnishings /hard porous / non-porous surfaces.

FS 9 Do not apply to those surfaces / on which food / feed is stored, prepared / or / eaten / which children are likely to touch.

FS 10 Do not prepare / use/ place bait / dust in / domestic kitchens / larders / food cupboards / where human or animal food or water could become contaminated.

FS 11 Do not use / spray in wet weather / strong winds / directly into breeze / wind.

FS 12 Avoid all contact by mouth / with skin / eyes.

FS 13 Avoid contact during pregnancy.

FS 14 Wear suitable respiratory equipment* / protective gloves / synthetic rubber gloves / PVC gloves / goggles / face shield / sou'wester / overalls / apron / impervious apron / mackintosh / boots / impervious boots / spray mask / dust mask / protective clothing (coveralls) / gauntlets and eye protection when handling / diluting / applying / spraying / dipping / using / removing / mixing the concentrate / liquid / dust / fumigant / bait / product / treated seed / freshly treated timber / trays / solution / growths from treated surfaces / and during maintenance of treatment equipment.

* a suitable type of respirator and canister should be specified.

or

Wear suitable protective clothing (coveralls) / suitable protective gloves / suitable respiratory protective equipment* when handling the concentrate / during application by hand-held equipment / during application by tractor drawn / mounted equipment

* dust mask

FS 15 Do not breathe dust / mist / smoke / fog / aerosol. (If necessary for personal comfort, wear a mask)

or

Avoid working in spray mist / smoke / fog.

FS 16 Wash off splashes immediately.

or

Wash splashes / dust / powder / concentrate / any contamination / paste / gel / from skin and eyes immediately.

FS 17 Wash hands and exposed skin / before eating, drinking or smoking and after work / before meals and after work / after use / handling

or

Wash hands before meals and after work.

FS 18 Extinguish all naked flames / including pilot lights / when applying the fumigant / dust / liquid / product.

FS 19 Do not apply /spray in the presence of / avoid / naked flames, hot surfaces / or / unprotected electrical equipment / any incandescent material.

FS 20 Do not work in confined spaces or enter spaces in which high concentrations of vapour are present. Where this precaution cannot be observed distance breathing or self-contained breathing apparatus must be worn, and trained operators should do the work.

FS 21 Ensure adequate ventilation when handling / applying (in confined spaces) / before and after treatment.

or

Wear (suitable) respiratory equipment during work in poorly ventilated areas / such as powered filtration or airline respiratory equipment with combined protective helmet and visor when spraying.

FS 22 Wash all protective clothing thoroughly after use, especially the insides of gloves.

or

Avoid excessive contamination of overalls / clothing and launder regularly.

FS 23 Do not handle seed unnecessarily.

FS 24 Not to be used as food or feed.

FS 25 Do not re-use sacks or containers that have been used for treated seed for food or feed.

or

Keep treated seed secure from people, domestic stock / pets and wildlife at all times during storage and use.

FS 26 Do not allow ... (product) ... to come into contact with food or cooking utensils.

or

Do not use on filter beds or sewage treatment works / internal timbers / suspended nests / uncovered food or grain, in grain storage or on food contact surfaces.

FS 27 Protect / cover food preparing equipment and eating utensils from contamination during application / before spraying.

or

Do not contaminate foodstuffs, eating utensils or food contact surfaces / other than storage boxes or containers / outdoor tables.

FS 28 Do not exceed use of one unit / strip per ... cu m (cu f).

FS 29 Do not apply more than ..... per (state amount).

FS 30 Do not apply more than ..... times per crop / season / time period.

FS 31 Keep children / pets / animals away from treated areas / baits for ..... hours / days / until dry.

FS 32 Remove / cover all / food / food processing equipment / eating utensils / foodstuffs / fish bowls / fish tanks / caged birds / pets / water storage tanks / before spraying / application / dusting / treatment.

FS 33 Protect exposed water / feed /milk machinery / milk containers from contamination.

or

Do not place bait / dust / gel in larders / food cupboards where human / or animal food / feed or water could become contaminated.

FS 34 Do not prepare / use / lay baits / dust / spray /operate dispenser where food / feed / water could become contaminated / in kitchens / or larders (when unwrapped food is stored) / in occupied hospital wards / in hospital operating theatres.

or

Do not use below level of damp proof course / in any buildings when livestock or other animals are kept or housed / as a broadcast treatment.

FS 35 Remove exposed milk / collect eggs before application.

or

Remove / all animals / pets / livestock / feed / exposed water / milk / collect eggs before application / spraying.

FS 36 Fumigate only under conditions that allow no leakage of gas to adjacent occupied premises.

or

Keep animals / birds out of premises where grain is under fumigation or being aired following fumigation.

FS 37 Do not harvest / crops for human / animal consumption / for at least (..... days/weeks) after last application.

or

Do not pick / gather / food / crops within ..... hours / days / weeks of treatment.

FS 38 For use on the following crops with stated minimum interval between last application and harvesting. Any table prepared should be based on cleared uses for the product in question. This safety information may be combined on the label with that on the efficient use of the product.

FS 39 Keep children / unprotected persons / livestock / pets / animals out of treated areas / for at least ..... (interval) / until walls / surfaces are dry / until / smoke has cleared / product / any product residue / the dust has been removed.

or

Ensure there is a physical barrier to prevent contact by unprotected persons and animals until treated surfaces are dry.

FS 40 Dangerous / Harmful to livestock. Keep all livestock / out of treated areas / away from treated water / for at least .... (interval). Bury or remove spillages.

or

Keep livestock out of treated areas for at least ..... (interval) / if poisonous weeds such as ragwort are present.

FS 41 Ventilate treated areas / rooms / confined spaces thoroughly / before occupying / after application when gas / smoke has cleared.

FS 42 Prevent access to baits by children, domesticated animals and pets, (particularly cats, dogs and pigs).

or

Keep / apply / suspend only in positions inaccessible to children and pets.

FS 43 Use bait containers clearly marked "Poison" at all / surface baiting points.

FS 44 Remove all remains of dust / bait / and bait containers / and dead rodents / after / at end of / treatment and burn / bury / destroy / dispose of safely.

or

Remove exposed dust thoroughly after use and bury / burn.

FS 45 Do not sow / plant / transplant .... (specify crops) ..... for at least ..... (interval).

FS 46 Do not use indoors / outdoors.

or

For indoor / outdoor use only.

FS 47 Do not use in occupied dwelling-houses / on internal timbers or residential property.

FS 48 Do not apply / treated seed from aircraft / the air / in and around drains.

FS 49 Dangerous / Harmful to game / wild / caged / birds / butterflies / animals / fish / bees / pets / bats. Bury spillages / Do not apply within reach of domestic animals / where animals may lick / come in contact with freshly treated surfaces.

or

High risk / Risk to non-target insects or other arthropods. Do not spray within 6m of the field boundary / See directions for use ./ For advice on use on Integrated Pest Management (IPM) see directions for use / general information.

FS 50 Dangerous / armful to bees. Do not apply / dust / spray / at flowering stage / crops in open flower / during bee activity. Keep down flowering weeds.

or

High risk to bees. Do not apply / spray / dust to crops / plants in flower or to those in which bees are actively foraging / except as directed on ….(crop) / Do not apply when flowering weeds are present.

FS 51 Extremely dangerous / Dangerous / Harmful to fish / and other aquatic life. Do not contaminate watercourses or ground / ponds, waterways / surface waters or ditches with the chemical or used container / The maximum concentration of active substance in treated water must not exceed (specify) ppm or such lower concentration as the appropriate water regulatory body may require.

or

Do not contaminate ponds, waterways or ditches with chemical or used container.

FS 52 Prevent any surface run off to / from entering storm / drains.

or

Avoid contamination of watercourses / ground.

FS 53 This material and its container must be disposed of in a safe way.

or

Dispose of used generator / contents of trap / baits / mats / coils and packaging safely.

FS 54 All washable containers should be labelled: Wash out container thoroughly / empty washings into spray tank / and dispose of safely / dispose of as follows: ..... (specify).

or

Rinse container thoroughly by using an integrated pressure rinsing device or manually rinsing three times. Add washings to sprayer at time of filling and dispose of safely/as follows ….. (specify).

FS 55 All non-washable containers should be labelled: Empty / and return used / container (completely) and dispose of safely / dispose of as follows: ..... (specify) / in a safe way.

or

Return empty container as instructed by supplier.

FS 56 Handle with care and mix only in closed container.

FS 57 Keep off skin / away from eyes.

FS 58 Avoid contaminating food

FS 59 Open containers outdoors / only as directed. (Protect from contact with moisture and keep away from burning or glowing material.

FS 60 Apply solutions from unbreakable containers carrying a pouring tube or similar device.

FS 61 Air / ventilate animal feed for at least ..... hours following fumigation.

FS 62 Keep animals / birds / out of premises where grain is under fumigation or being aired / ventilated following fumigation.

FS 63 Remove excess dust and air treated fabrics thoroughly before use.

FS 64 Search for and burn / bury all rodent bodies. Do not place in refuse bins or on rubbish tips.

FS 65 Spray only into the air / onto surfaces.

FS 66 Do not handle treated fabrics / nets until dry and air thoroughly before use.

FS 67 Avoid skin contact with / do not wear / freshly treated clothing.

FS 68 Do not use on beehives / beekeeping equipment.

FS 69 Avoid (direct) contact with plant life / leaves of growing plants (until solvent has evaporated).

FS 70 Dispose of surplus chemical / contaminated materials (including sawdust) and empty the container safely using a method approved by the Waste Disposal Authority.

FS 71 Sawdust from treated timber should be treated as contaminated waste and disposed of safely.

FS72 Treated wood / trays should not be used or dispatched / handled until surfaces are dry / at least 48 hours after treatment

or

Treated wood should be held under cover (with adequate ventilation)/up to 48 hours / or until dry, before dispatch (or erection)

FS 73 Do not allow direct spray from ground crop sprayers to fall within 5m / (specify) m / of the top of the bank of a static or flowing water body or within 1m / (specify) m / of the top of a ditch that is dry at the time of application. Direct spray away from water.

or

Do not allow direct spray from hand-held sprayers to fall within 1m of the top of the bank of a static or flowing water body. Direct spray away from water.

FS 74 Users must consult the appropriate local authority (County Council or Corporation) before using the product near water and must obtain their agreement before using this product to control aquatic weeds.

FS 75 Medical Advice.

Situations will arise where it is either desirable or necessary that medical advice additional to that provided in the context of safety phrases S 26, S 44, S 45, and S 46 be provided on labels. In such cases the following criteria apply:

Further Advice Poisons Information Centre, Beaumont Hospital, Dublin 9.
Telephone: 01-837 99 64 and 01-837 99 66

Organophosphorous plant protection products

Symptoms	These may include sweating, headache, weakness, faintness and giddiness, nausea, stomach pains, vomiting, small pupils, blurred vision, muscle twitching.
First Aid	If any of the above symptoms occur, particularly if there is known contamination; stop work; remove contaminated clothing; wash exposed skin and hair; prevent all exertion; and call doctor at once and show him the label.

Guide to Doctor

Specific treatment	1	Where signs and symptoms are present and as early as possible, inject treatment atropine sulphate 2 mg or pro rata for children and repeat (if necessary) until fully atropinised.
	2	If available administer pralidoxine 1g by intra-muscular injection. Repeat after 3-4 hours.
Other measures	1	Keep airway clear.
	2	Watch respiration - intubation with endotracheal tube, or tracheotomy may be necessary in conjunction with artificial ventilation.
	3	Put patient at complete rest in hospital for 24 hours at least.
Confirmation of Diagnosis	Estimate cholinesterase activity (5 ml blood unhaemolysed, collected in an anticoagulant).	

Carbamate plant protection products

Symptoms — These include excessive sweating, headache, weakness, faintness and giddiness, nausea, stomach pains, vomiting, small pupils, blurred vision, muscle twitching.

First Aid — If any of the above symptoms occur, particularly if there is known contamination; stop work; remove contaminated clothing; wash exposed skin and hair; prevent all exertion; call doctor at once and show him the label.

Guide to Doctor

Specific treatment
1. Where signs and symptoms are present and as early as possible inject atropine sulphate 3 mg or pro rata for children and repeat if necessary until fully atropinised.
2. Do not use pralidoxine.

Other measures
1. Keep airway clear.
2. Watch respiration - intubation with endotracheal tube or tracheotomy may be necessary in conjunction with artificial ventilation.
3. Put patient at complete rest in hospital for 24 hours at least.

Bipyridyl plant protection products

Symptoms — Following ingestion, nausea, vomiting, abdominal pain and diarrhoea (often bloody) may occur within a few hours and result in severe fluid and electrolyte disturbance. In severe cases, circulatory collapse and coma may occur. The concentrate may cause irritation to skin and eyes.

First Aid — Wash concentrate or spray from skin immediately; wash eye splashes with water for 10 to 15 minutes and seek medical attention; if swallowed, induce vomiting, if not already occurring and take patient to hospital immediately.

Guide to Doctor

Specific treatment
1. Give stomach washout and at the same time test urine and gastric aspirate for the presence of paraquat or diquat.
2. If the test is positive, purge the gastrointestinal tract immediately with up to one litre of a 15% suspension of Fuller's Earth and 200 ml of 20% mannitol in water.
3. Give a sodium or magnesium sulphate purgative separately.
4. Contact the Poisons Information Centre for further advice on treatment.

Test - quick qualitative — Paraquat and diquat can be detected by reduction to blue or green radical ion with sodium dithionite under alkaline conditions.

Quick test capsules can be prepared by mixing the following materials:

Sodium dithionite (hydrosulphite)	10 g
pH buffer powder	6 g
Sodium bicarbonate	25 g

The reagents, thoroughly mixed, and packed in 1 g amounts in gelatine capsules (gauge 0) can be stored at room temperature in a screw-capped container for at least six months.

The test is performed by breaking open the capsule and tipping the contents into 10ml of urine, and shaking gently until dissolved. A green or blue colour indicates the presence of paraquat or diquat.

Appendix 13

Regulation 6 (2)

GOOD PLANT PROTECTION PRACTICE

Introduction

(i) These principles of Good Plant Protection Practice (GPP) provide the basis for the identification of optimal practice in the use of plant protection products. GPP includes principles concerning use of individual products in the context of overall plant protection programmes. It provides a practical standard for assessing individual practices, with efficacy, human health, animal health and environmental safety being the principal endpoints.

(ii) In the context of the provisions of Regulation 6, the conditions of authorization and the conditions of use reflected on approved labels, the principles of Good Plant Protection Practice, define the uses and manner of use that are permitted (see Regulation 6).

(iii) Within the limits established in the context of the uses for which individual plant protection products are authorized and the conditions and restrictions associated with each such authorization, the principles of good plant protection practice provide the basis for:

a) the choice of active substance and formulation;

b) the choice of -

- dosage (and if appropriate volume),
- the number of applications to be used,
- their timing,
- the application equipment to be used and the method of application,

in the context of -

- crop factors (*e.g.* cultivar, sowing rate, timing of sowing, fertilization regime, training system, age, spacing),
- climatic and edaphic factors (*e.g.* topography, soil type, rainfall, temperature, light).
- possibilities for cultural and biological control,
- cost effectiveness,
- the harmful organism spectrum to be controlled,
- compatibility between products and identified side-effects,

providing an overall and rational schedule for treatment with plant protection products, timed partly by the calendar, partly by crop growth stage/phenology and partly by specific harmful organism warning systems, incorporating as appropriate other means of protection, such that efficacious control of the whole harmful organism spectrum (*e.g.* pest/disease/weed) is achieved, with the minimum amount of product usage.

(iv) While Good Plant Protection Practice, permits the use of reduced rates of application and use of products in tank mixes, in certain specified circumstances, it does not permit use of plant protection products for purposes for which the product was not authorized, unless an extension of the field of application of an authorized product has been granted in accordance with Regulation 16 for the use concerned. Good Plant Protection Practice does not permit use at rates of application higher, or frequencies more often, than provided for in the conditions of authorization and the conditions of use reflected on approved labels or than provided for in granting extensions of the field of application of authorized products.

(v) Good Plant Protection Practice includes use, where possible, in accordance with the principles of integrated control.

General principles

These general principles of GPP must be read in conjunction with the European and Mediterranean Plant Protection Organization (EPPO) specific principles of GPP, where available. They are intended to serve as an aid for the use of the individual crop-specific guidelines. They include points which are not necessarily repeated in the specific guidelines, but which apply in general to all.

1 *Crop factors and cultural control*

1.1 GPP depends first on good agricultural practice in the everyday sense, which is referred to as "good standard practice" in the EPPO Standards on efficacy evaluation of plant protection products. Crops should be well managed according to local practice. Measures applied should be cost-effective in relation to the value of the crop. Sowing or planting material should be healthy and general hygiene should be maintained. Resistant or tolerant cultivars should be used if available and the crop should be grown in a manner that minimizes the need for product inputs (*e.g.* rotation sequence, elimination of weeds as potential sources of infection). However, this can only be stated very broadly. Farmers and growers may wish to grow a highly susceptible cultivar because of its high quality, or use a certain fertilization regime, sowing rate, pruning system . or other technique, because it favours high yield or the achievement of the required quality of produce.

1.2 'Integrated production' systems seek to optimise all aspects of crop management to ensure best quality. Similarly 'organic farming' takes advantage of a wide range of cultural practices to achieve its particular aims. The scope of GPP embraces those systems of production, provided that the conditions of registered use are respected for any substances used for plant protection and acceptable efficacy in plant protection is ensured. Cultural practices can, however, be successfully used in GPP without calling on such systems.

1.3 Plant protection practices selected must be safe for the crop to be treated. It is evidently GPP to avoid products that are phytotoxic to species or cultivars, an aspect that generally is covered by the conditions of authorization for individual plant protection products.

2 *Local pest spectrum to be controlled and thresholds for action*

2.1 In a given crop, only certain pests are likely to occur. The spectrum of harmful organisms requiring control varies regionally, and depends on climatic conditions, soil type and other factors. Thus GPP is conditioned by control needs. In a given region, various indices can be used to determine whether a given harmful organism will need to be controlled in a given season - population levels at the end of the previous season, threshold levels at the beginning of the season, occurrence of weather and other conditions essential for development of the harmful organism.

Therefore, going further than just the timing of applications, GPP seeks to establish whether a harmful organism needs to be controlled or not.

2.2 The importance of particular harmful organisms varies from season to season, and plant protection products are generally active against a spectrum of harmful organisms. In general, it is better GPPP to use one product that is active simultaneously against two or more harmful organisms, if the treatments can be correctly timed, than to treat them separately with two or more products. However, against a single harmful organism, a more specific product is to be preferred to a broad-spectrum product.

3 *Conditions of authorization of plant protection products*

The conditions and restrictions associated with individual authorizations granted, establish limits on the uses for such products. This ensures that maximum residue limits are respected and that any environmental effects are kept to a minimum. Use other than in accordance with those limits is, by definition, never GPP. However, it is not GPP to operate at or near those limits, where, for instance in particular situations, the use of fewer applications, lower rates of application or longer intervals between last application and harvest provide satisfactory plant protection. The aim of GPP is to ensure use in accordance with a concept of adequate effectiveness having regard to cost/benefit, using a range of control methods not just plant protection products.

4 *Choice of active substance and formulations*

4.1 The choice of active substances and formulation to be used in a particular situation is constrained by a number of elements. There is not a GPP principle that it is better to use few or many active substances, or one type of formulation rather than another. Each formulated product is characterized by its efficacy profile, its cost and the side-effects that result from its use.

4.2 The first choice to be made is whether or not it is indeed necessary to use a plant protection product. Where an effective and economically viable alternative exists in the particular plant protection situation concerned, there is no need to use a plant protection product. If, however, it is necessary to use a plant protection product and a choice has to be made between active substances and/or formulations, it is preferable, subject to the over-riding consideration of acceptable efficacy against the plant pest spectrum concerned, to use -

- products that lead to fewer or less severe side-effects (*i.e.* non-persistent products) and which are safer for the environment,
- selective plant protection products rather than broad-spectrum products, and
- plant protection products that involve a lesser risk of the development of resistance (also see point 12).

4.3 It can be GPP to use products in tank mixes (including tank mixes with adjuvants and fertilizers), since by reducing the number of spray applications, the extent of operator exposure, fuel use, passage through the crop, *etc.*, can also be reduced. However, it is known that certain tank mixes can have negative effects. It is therefore important to ensure that the timing of the application is still consistent with the GPPs for the products separately, that the products are compatible one with another, and that their individual efficacy and crop safety performances are not diminished. This is often specified through the conditions associated with authorizations granted, but is not always so specified. In situations not addressed on product labels, it is GPP to use products in a tank mix, where on the basis of good experimental evidence relating to the range of conditions arising, generated over at least two growing seasons, their compatibility has been established and through the use of a tank mix economies can be achieved.

4.4 It is GPP to use an authorized adjuvant with particular plant protection products, where such use is in accordance with the conditions of the authorizations concerned, or where on the basis of good experimental evidence relating to the range of conditions arising, generated over at least two growing seasons, it has been established that through use of an adjuvant, the effectiveness of the plant protection product is enhanced, or the dosage of the plant protection product may be reduced. It is not GPP to use an adjuvant with a plant protection product in such a manner that residues of the plant protection product at harvest or following storage are increased. It is not GPP to use an adjuvant that has not been authorized for use with plant protection products.

5 *Choice of dosage*

The maximum dosage permitted is fixed by the conditions associated with authorizations granted and may provide for several different dosage depending on circumstances arising.. It is not GPP to use higher doses (as they are not authorized and such use is therefore illegal). A low-dosage (lower, reduced) treatment may be considered GPP if there is good experimental evidence relating to the range of conditions arising, generated over at least two growing seasons, to show that it is effective in the specific conditions encountered. The EPPO Standard on "Minimum effective dose" provides relevant detailed guidance.

6 *Choice of volume*

For tall-growing crops, it is important to apply sprays at the correct dose – volume may also be important. For such crops, dosage and volume are generally specified and differentiated on the basis of crop size.

7 *Number, timing and frequency of applications*

7.1 It is GPP to achieve adequate control by applying only as many treatments as are needed for effective control. This number may vary considerably between seasons and localities. Monitoring and forecasting systems are important elements providing information necessary for the decision whether or not and when chemical control measures should be applied

7.2 The timing of the first application so that it is neither wastefully too early, nor too late (allowing populations to build up) is a key element in GPP. Numerous warning systems exist which allow forecasts to be made as to when individual harmful organisms will become active (meteorological, direct monitoring, pheromone traps *etc.*). In any event, and especially if direct warnings are not available, account must be taken of local experience, especially of advisory services and farmers and overall visual observation. If practicable and reliable control thresholds are available, they should be used to determine the necessity for and time of plant protection measures, as possible for each individual field

7.3 It may be possible to continue to use warning systems to time subsequent applications (against successive generations of an insect, or by detecting infection periods for fungi). It is GPP to do this as far as is practicable. It should, however, be noted that generations may come to overlap, or overall weather conditions may favour a disease over a long period.

7.4 There are frequently situations when the only possible GPPP is to treat regularly. It is not GPP to develop a warning system that is impractically complicated, especially if it does not succeed in reducing the number of applications below those of a reasonable calendar programme. Treating according to a fixed programme of dates, or of phenological stages of the crop, is consistent with

GPP, unless it has clearly been shown that it is possible and practical to use a warning system to reduce the number of applications in most years.

7.5 Some treatment regimes allow for an interaction of dosage and frequency (higher dose less often, lower dose more often, subject to the limits specified on labels). There is no particular GPPP preference in this respect.

7.6 The timing of the last application will be determined by what is needed for effective control, subject to the over-riding condition that the pre-harvest interval be respected. In many cases, it may be GPP to make the last application long before the latest date permitted in accordance with the pre-harvest interval specified.

8 *Equipment and method of application*

It is GPP to select equipment and application conditions that ensure that a high proportion of product applied reaches its target, with, for sprays in particular, the minimum wasted as aerial drift or onto the ground. Many factors must be taken into consideration (nozzle type, pressure, spray volume, droplet size, speed, *etc.*), in selecting the equipment and method of application to be used. However, in making such selections, for each product, care must be taken to ensure that efficacy is maintained. It is especially important that the equipment used be properly calibrated and that the calibration be regularly checked, to ensure that the correct dosage is applied.

9 *Biological means of control*

9.1 The concept of GPP relates to plant protection products in general, including formulated products containing micro-organism and natural enemies that may be introduced into a crop (*e.g. Encarsia formosa* in glasshouses). Such biological means of control form, in appropriate cases, an essential element of GPP. GPP is concerned with the proper use of such products, and with the interaction between them and natural enemies introduced into a crop. There must be good experimental evidence that such biological means of control have an acceptable degree of efficacy.

9.2 GPP also seeks to derive benefit from the management of natural enemies that pre-exist in a crop. In particular, GPP must respect the conditions of authorization relevant to use, which seek to protect natural enemies. If reliance on a biological agent (*e.g.* typhlodromid mites in orchards) has become a regular component of the control scheme within a crop, then it is GPP to avoid products that would destroy the agent and thus lead to a need to use more of other products.

10 *Integrated control*

10.1 The term *integrated control* is defined as the rational application of a combination of biological, biotechnological, chemical, cultural or plant-breeding measures whereby the use of chemical plant protection products is limited to the strict minimum necessary to maintain the pest population at levels below those causing economically unacceptable damage or loss.

10.2 Most of the elements of that definition also apply to GPP. Plant protection practice based on integrated control methods is GPP and, as such, is recommended. However, the principles of GPP do seek to reduce the use of chemical plant protection products to a strict minimum, only to avoid any and all unnecessary use.

11 *Identified side-effects*

Side-effects on bees, or on wildlife, are covered by the conditions of authorization for individual products, so GPP will automatically take account of them. Side-effects on natural enemies of harmful organisms, which interact with the efficacy of plant protection products have been addressed (*cf* point 9 - Biological means of control). It is GPP to seek and consider all up-to-date information on such side-effects. The EPPO Standard PP£ Environmental risk assessment of plant protection products provides a system for evaluating all such side-effects.

12 *Risk of resistance*

An important side-effects of product use is the coincidental imposition of selective pressure for the development of resistant harmful organism populations. It is GPP to take full account of all reports on appearance of practical resistance and to consider the properties of other active ingredients of the same chemical type. For particular crops, with their harmful organism spectra, recommendations may be made on a resistance avoidance strategy *e.g.* recommendation to not use one class of fungicide continually against foliar diseases as that would select out strains that will attack the crop later in the season; to use a "sensitive" product not more than once a season; to use formulations having more than one active substance, particularly those with a multi-site mode of action or a range of modes of action; to use other methods of control. Guidelines for different groups of plant protection products have been developed by the *Resistance action committee* of CropLife International: FRAC (for fungicides); IRAC (for insecticides); HRAC (for herbicides). EPPO Standard PP 1/213 Resistance risk analysis also provides relevant guidance. Where such strategies have been defined, it is GPP to follow them.

13 *Safety*

GPP requires that relevant statutory requirements and official codes of practice for the safety of the operator, consumer and environment, be respected.

14 *Training and documentation*

14.1 It is GPP to ensure that all applications of plant protection products are made by trained operators. Relevant statutory requirements and official codes of practice in relation to training of operators must be respected.

14.2 It is GPP to document all applications of plant protection products on-a field by field basis and to retain such records for a at least five years.

Appendix 14

Regulation 8 (2)

REQUIRED FORMAT FOR PRESENTATION OF DOCUMENTATION

1 The format for the presentation of the documentation referred to in paragraph (2) of Regulation 8 is that described in the "Guidelines and Criteria for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for the Inclusion of Active Substances in Annex I of Directive 91/414/EEC (Article 5.3 and 8.2)", as amended from time to time [73]. Alternatively, the OECD guidance for industry data submissions on plant protection products and their active substances (Dossier Guidance) [74] can be used. The OECD format should be used in the case of dossiers compiled after 1 January 2003.

2 Where in accordance with Regulation 10, it is claimed that particular tests or study reports be protected, the owner of the tests or studies concerned must be indicated. Where ownership is shared, all of the joint owners must be identified.

3 Where in accordance with sub-paragraphs (1) (a) and (3) (a) of Regulation 10, agreement to the use of information submitted by other parties is claimed, an original signed and notarised letter, confirming such agreement, and submitted by the owner of the information, must be provided. Each such letter must include the following information:

(i) the identity of those to whom agreement for the use of information submitted has been granted;

(ii) the purposes for which such agreement has been granted (a particular product, a group of products, or all relevant products); and

(iii) the period for which the agreement given is valid.

4 In the case of existing active substances being reviewed for possible inclusion in Annex I, or being reviewed in the context of applications for authorization of preparations in accordance with Regulation 18, where the information qualifies for protection pursuant to Regulation 10 of the principal Regulations, the following must be provided:

(i) for each test and study referred to in sub-paragraph (1) (c) of Regulation 10, a list of the Member States in which one or more preparations containing the active substance was on the market on 24 July 1993, and the dates on which authorization of the first such preparation was granted by each such Member State - in the case of preparations placed on the market prior to 2 December 1985 in Ireland and prior to 6 October 1986 in the UK, the dates of first placing on the market - and the date of expiry of the period of protection for each Member State;

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[73] European Commission Document 1663/VI/94 Rev 8, 22 April 1998

[74] Guidelines and criteria for industry for the preparation and presentation of complete dossiers and summary dossiers for plant protection products and their active substances in support of regulatory decisions in OECD countries, Revision1, March 2001, http://www.oecd.org/oecd/pages/home/displaygeneral/0,3380,EN-document-527-14-no-4-29024-0,00.html

(ii) for each test and study referred to in sub-paragraph (1) (b) of Regulation 10, a statement that the test or study was generated for the purposes of achieving inclusion in Annex I or has not been previously submitted to the competent authorities of any of the Member States for the authorization of a plant protection product;

(iii) for each test and study referred to in sub-paragraph (3) (b) of Regulation 10, the identity of the first Member State to authorize the preparation, the date of authorization and the date of expiry of the period of protection for the Community; and

(iv) for each test and study referred to in sub-paragraph (3) (c) of Regulation 10 a list of the Member States in which the preparation was authorized, and the dates on which such authorization was granted by each such Member State - in the case of preparations placed on the market prior to 2 December 1985 in Ireland and prior to 6 October 1986 in the UK, the dates of first placing on the market - and the date of expiry of the period of protection for each Member State.

Appendix 15

Regulation 16 (2)

DOCUMENTATION AND INFORMATION TO SUPPORT APPLICATIONS FOR AN EXTENSION IN THE FIELD OF APPLICATION OF A PLANT PROTECTION PRODUCT INCLUDED ON THE REGISTER OF PLANT PROTECTION PRODUCTS

1 Introduction

1.1 In principle, the information and data requirements relating to human and animal safety, relating to fate and behaviour in the environment and relating to impact on non-target species, necessary to support applications for an extension in the field of application of a plant protection product included on the register of plant protection products, are the same as those required to support applications for the authorization of the product concerned for the additional uses, while the data and information requirements relating to efficacy are much less onerous.

1.2 In practice, in most cases, much of the data relating to human and animal safety, relating to fate and behaviour in the environment and relating to impact on non-target species, will have been supplied by, or on behalf of, the applicant(s) for inclusion of active substances concerned in Annex I and/or on behalf of the authorization holder, the data and information required for an extension in the field of use is much less extensive than for the authorization of the product concerned for the additional uses.

1.3 The information and data required and specified in this Schedule, is limited to that which either will always be required, or which may be required, depending on:

(i) the nature of the proposed use;

(ii) the nature and properties of the plant protection product; and

(iii) the nature and extent of the data and information provided by, or on behalf of the applicant(s) for inclusion of active substances concerned in Annex I and/or by or on behalf of the authorization holder, or where relevant, the holder of the permission to market or notification.

1.4 Since applicants may not be aware of the extent and nature of the data provided by, or on behalf of, the applicant(s) for inclusion of active substances concerned in Annex I and/or on behalf of the authorization holder, they should consult the competent authority before undertaking work necessary for the generation of the data required to support applications.

1.5 In accordance with Regulation 16, extensions in the field of application can only be granted where the uses concerned are minor in nature. Minor uses can be any use on a crop grown to a very limited extent within the territory of the State, or a minor use on crops grown more extensively, taking into account, in the case of food crops, the dietary significance of the food commodity concerned.

2 **Efficacy data requirements**

2.1 Although a full programme of trials relating to the performance of plant protection products, in terms of their efficacy for the proposed uses and possible phytotoxicity, is not required, sufficient evidence must be provided to establish that it is in the public interest that the extension in the field of use concerned, be granted. The main requirements, in that regard, are:

(i) to demonstrate that crops, plants or plant products cannot be satisfactorily protected by other available means, at an economic cost; and

(ii) to establish that following use as proposed, the desired effect can be achieved without damage to the crop, plants or plant products treated.

2.2 In some cases, it will be possible to fulfil the requirements on the basis of extrapolation from and comparisons with existing authorized uses, or uses authorized in other Member States for the plant protection product or similar plant protection products. Where on the basis of comparisons and extrapolations, it is not established, to the satisfaction of the competent authority, that the plant protection product concerned will provide satisfactory results when used as proposed, a limited programme of trials, conducted in accordance with the requirements of Section 6 of Annex III and with those specified in the Sixth Schedule, should be undertaken and reported.

3 **Residues data requirements**

3.1 The consideration of applications for extensions in the field of use of authorized plant protection products, must take account of relevant statutory provisions concerning pesticide residues in food and feed. It is necessary that for each extension in use to be granted,

(i) it be demonstrated that existing Maximum Residue Levels (MRLs) will be respected following use as proposed, or

(ii) sufficient data is provided to support the establishment, on a provisional basis, of a different Community MRL in accordance with the Directive of 1991.

3.2 The requirement specified in subparagraph 3.1 (i) to demonstrate that existing MRLs will be respected can be satisfied through provision of -

(i) a sufficient quantity of relevant supervised trials data, or

(ii) the results of national or Community pesticide residue monitoring relevant to samples taken in regions where the proposed use is authorised or permitted and where the analytical screen includes residues of the active substance concerned, or

(iii) evidence of authorization for the use concerned granted following application of the Uniform Principles (*cf* Annex VI) in another Member State,

(iv) evidence of authorization, registration or off-label approval for the use concerned granted in another Member where relevant supervised trials data were required to support the application for the authorization, registration or off-label approval granted.

3.3 Existing Community rules relating to the extrapolation of data from crop to crop may serve to preclude the need for or minimize the extent of the data required (*cf* guidance on regulatory testing procedures for residues of plant protection products in food [54]). In other cases, the authorization holder may have the necessary data on file, and if requested by the applicant, may

be prepared to submit it in support of an application for an extension in the field of use of the product concerned.

3.4 In all cases in which applicants consider that residue data may be required, they should consult the competent authority prior to undertaking any programme to generate such data, as data of which the applicant is unaware, which might serve to preclude the need for or reduce the extent of any additional data required, may be available to the competent authority.

3.5 Where it is necessary to generate data relating to residues in food or feed products, the necessary supervised trials must be conducted and be reported in accordance with the requirements specified in Section 6 of Annex II and Section 8 of Annex III. Since the data to be generated should relate to all relevant parts of the Northern and Central Europe region, where use is envisaged, not just to Ireland, the necessary trials programmes should be designed to take account of the range of factors affecting variability in that region. Accordingly, applicants should co-operate with counterparts in other Member States, to ensure that data relevant to the necessary range of conditions is generated and duplication of effort is avoided.

Appendix 16

Regulations 25 (1) and 26 (4)

Principles of Good Experimental Practice

1 Introduction

The prime purpose of the Principles of Good Experimental Practice (GEP) is to promote the development of quality test data. A further objective is to facilitate the mutual acceptance of test data for regulatory purposes by other Member States of the Community, thereby avoiding duplicative testing and achieving economies in test costs and time, where test conditions are shown to be comparable. The Principles of Good Experimental Practice are analogous to the Principles of Good Laboratory Practice (GLP). They are designed to facilitate the production of quality data, generated through testing at many sites, including those that are not directly controlled by those conducting tests, without imposing impractical quality assurance and inspection obligations.

These Principles of Good Experimental Practice apply to the testing of the performance (efficacy and phytotoxicity) of plant protection products, including adjuvants, in support of applications for the authorization of plant protection products. These Principles also apply to the testing of both active substances and plant protection products, with respect to physical and chemical properties and technical characteristics, where the tests do not relate to their properties or safety with respect to human health or the environment.

Testing with respect to effects on honey bees and beneficial arthropods other then bees (*cf* paragraph 2.2 of the introduction to Annex II, and paragraph 2.4 of the introduction to Annex III), carried out in accordance with these Principles of Good Experimental Practice, as opposed to GLP, will be accepted if initiated prior to 31 December 1999.

Supervised residues trials relating to plant protection products containing active substances already on the market prior to 25 July 1993 (*cf* paragraph 2.3 of the introduction to Annex II, and paragraph 2.5 of the introduction to Annex III), conducted in accordance with these Principles of Good Experimental Practice, as opposed to GLP, will be accepted if initiated prior to 31 December 1997.

2 Definitions

2.1 *testing facility*: The persons, premises, and operational unit(s) necessary for testing. The term may include several sites, at one or more geographical locations, where phases or components of a single overall programme of tests are conducted. The different sites may include, but are not limited to:

- laboratory(ies) where the test or other material is characterized, measured, or otherwise assessed;
- one or more agricultural or other in- or outdoor sites, including glasshouses, where the test material is applied to the test system; and

- where relevant a processing facility where harvested commodities are treated to prepare other items, *e.g.* conversion to sugar, flour, beer, puree, juice.

2.2 *test*: Technical operation that consists of the determination of one or more characteristics or effects of a given active substance, plant protection product, or adjuvant, according to a specified procedure.

3 Legal Identity

The testing facility shall be legally identifiable.

4 Impartiality, independence and integrity

The testing facility and its personnel shall be free from any commercial, financial and other pressures that might influence their technical judgement.

Any influence on the results of examinations and tests exercised by persons or organizations external to the testing facility shall be excluded.

The testing facility shall not engage in any activities that may endanger the trust in its independence of judgement and integrity in relation to its testing activities.

When products are tested by bodies, which have been or are concerned with their design, development, manufacture or sale, provision shall be made for a clear separation of the different responsibilities and for an appropriate statement as to responsibilities.

5 Technical competence

5.1 *Management and organization*

The testing facility shall be competent to perform the tests concerned. In the absence of a recognized test guideline, agreement between the client and the testing facility to the test procedure shall be documented.

The testing facility shall be organized in such a way that each member of personnel is aware of both the extent and the limitation of his area of responsibility.

The organization shall provide supervision by persons familiar with relevant test methods and procedures, the objective of such testing and the assessment of test results. The proportion of supervisory to non-supervisory personnel shall be such as to ensure adequate supervision.

The testing facility shall have a technical manager who has overall responsibility for the technical operations of the facility.

A document showing the organization and distribution of responsibilities of the testing facility shall be available and kept up-to-date.

5.2 *Personnel*

The testing facility shall have sufficient personnel, having the necessary education, training, technical knowledge and experience for its assigned functions.

The testing facility shall ensure that the training of its personnel is kept up-to-date.

Information on the relevant qualifications, training and experience of the technical personnel shall be maintained by the facility.

5.3 *Premises and equipment*

5.3.1 *Availability*

The testing facility shall be furnished with all items of equipment required for correct performance of the tests and measurements which it claims to be competent to carry out.

In the exceptional case where the facility is obliged to use outside equipment, it shall ensure the quality of that equipment.

5.3.2 *Premises and environment*

The environment in which the tests are undertaken shall not invalidate the test results or adversely affect the required accuracy of measurement. The premises shall have the equipment, energy sources and other services needed for the testing. When the testing so requires, they shall be equipped with devices to monitor environmental conditions.

Access to and use of all test areas shall be controlled in a manner appropriate to their designated purpose and conditions of entry by persons external to test sites shall be defined.

In the case of premises used by a testing facility that are not subject to the exclusive control of the testing facility, arrangements shall be made to control access to and use of test areas in a manner appropriate to their designated purpose. The conditions of entry by persons external to the testing facility and the means of ensuring compliance with those conditions shall be defined.

Adequate measures shall be taken to ensure good housekeeping in the testing facility.

5.3.3 *Equipment*

All equipment shall be properly maintained. Details of maintenance procedures shall be available.

Any item of the equipment which has been subjected to overloading or mishandling, or which gives suspect results, or has been shown by calibration or otherwise to be defective, shall be taken out of service, clearly labelled and stored at a specified place until it has been repaired and then shown by test or calibration to be performing its function satisfactorily. The testing facility shall examine the effect of this defect on previous tests and report its findings to the competent authority.

Records shall be maintained of each major item equipment used in testing. Each record shall include:

a) the name of the item of equipment;

b) the manufacturer's name and type identification and serial number;

c) date received and date placed in service;

d) current location, where appropriate;

e) condition when received (*e.g.* new, used, reconditioned)

f) details of maintenance carried out; and

g) history of any damage, malfunction, modification or repair.

Measuring, testing and dispensing (including application) equipment used in the testing facility shall be calibrated where appropriate before being put into service and thereafter according to an established programme.

The overall programme of calibration of equipment shall be designed and operated so as to ensure that wherever applicable measurements made in the testing facility are traceable to national and international standards of measurement. Where traceability to national or international standards of measurement is not applicable, the testing facility shall provide satisfactory evidence of correlation or accuracy of test results (for example by participation in a suitable programme of inter laboratory comparisons).

Reference standards of measurement held by the testing facility shall be used for calibration only and for no other purpose.

A competent body that can provide traceability to a national or international standard of measurement shall calibrate reference standards of measurement.

Where relevant, testing equipment shall be subjected to in-service checks between regular re-calibrations. The calibration of application equipment shall be checked on each occasion on which it is used in a test.

Reference materials shall where possible be traceable to national or international standard reference materials.

5.4 *Working procedures*

5.4.1 *Test methods and procedures*

The testing facility shall have adequate documented instructions on the use and operation of all relevant equipment, on the handling and preparation of test materials, and on standard testing techniques. All instructions, standards, manuals and reference data relevant to the work of the testing facility shall be maintained up-to-date and be readily available to the personnel.

The testing facility shall use methods and procedures required by or acceptable to the competent authority for the testing of plant protection products. The experimental protocol to be followed shall be provided to personnel performing the test, together with all relevant documented instructions on the handling and preparation of test materials, and on standard testing techniques.

The testing facility shall reject requests to perform tests according to test methods that may endanger an objective result, have a reduced validity or are unacceptable to the competent authority.

Where it is necessary to employ test methods and procedures that are non-standard, these shall be fully documented.

All calculation and data transfer shall be subject to appropriate checks.

Where results are derived by electronic data processing techniques, the reliability and stability of the system shall be such that the accuracy of the results is not affected. The system shall be able to detect malfunctions during programme execution, to permit appropriate action to be taken.

5.4.2 *Quality System*

The testing facility shall operate a Quality System appropriate to the type, range and volume and intended purpose of work performed. The elements of this system shall be documented in a Quality Manual that is available for use by the personnel responsible for and involved in testing. A nominated responsible member of the testing facility personnel shall maintain the Quality Manual current.

A person or persons having responsibility for quality assurance within the facility shall be designated by the facility management and have direct access to top management.

The Quality Manual shall contain at least:

a) a quality policy statement;

b) the structure of the laboratory (organizational charts);

c) the operational and functional activities pertaining to quality, so that each person concerned will know the extent and the limits of his responsibility;

d) general quality assurance procedures;

e) reference to quality assurance procedures specific for each test, as appropriate;

f) where appropriate, reference to proficiency testing, use of reference material, *etc.*;

g) satisfactory arrangements for feedback and corrective action whenever testing discrepancies are detected; and

h) procedure for dealing with complaints.

The quality system shall be systemically and periodically reviewed by or on behalf of management to ensure the continued effectiveness of the arrangements, and any necessary corrective action initiated. Such reviews shall be recorded together with details of any corrective action taken.

5.4.3 *Test reports*

The work carried out by the testing facility shall be covered by a report which accurately, clearly and unambiguously presents the test results and all other relevant information.

In addition to the information to be reported as specified in relevant test guidelines, each test report shall include at least the following information:

a) name and address of testing facility and the precise location where the test was carried out;

b) unique identification of the report (such as serial number) and of each page, and total number of pages of the report;

c) name and address of client;

d) description and identification of the test material;

e) date of receipt of test material and date(s) of performance of test;

f) identification of the test guideline or description of the method;

g) description of sampling procedure, where relevant;

h) any deviations, additions to or exclusions from the test guideline, and any other information relevant to a specific test;

i) identification of any non-standard test method or procedure utilized, and a full description of the test method;

j) measurements, examinations and derived results, supported by tables, graphs, sketches and photographs as appropriate;

k) a statement on measurement uncertainty (where relevant);

l) a signature and title or an equivalent marking of person(s) accepting technical responsibility for the test report and date of issue; and

m) a statement to the effect that the test results relate only to the items tested.

Particular care and attention shall be paid to the arrangement of the test report, especially with regard to presentation of the test data and ease of assimilation by the reader. The format shall

be carefully and specifically designed for each type of test carried out, but the headings shall be standardized as far as possible.

Corrections or additions to a test report after issue shall be made only by a further document suitably marked, *e.g.* "Amendment/Addendum to test report serial number...(or as otherwise identified)", and shall meet the relevant requirements of the preceding paragraphs.

A test report shall not include any advice or recommendation arising from the test results.

Test results shall be presented accurately, clearly, completely and unambiguously in accordance with instructions that may be part of the test methods.

Quantitative results shall be given together with calculated or estimated uncertainty.

NOTE: Test results could be measured values, findings from the visual examination or practical use of the test material, derived results or any other type of observation from the testing activities. Tables, photographs, or graphical information of any kind, appropriately identified, could support test results.

5.4.4 *Records*

The testing facility shall maintain a record system to suit its particular circumstances and comply with any existing regulations. It shall retain on record all original observations, calculations and derived data, calibration records and the final test report for as long as the substance or product concerned continues to be authorized or placed on the market in the Community. The records for each test shall contain sufficient information to permit repetition of the test. The records shall include the identity of personnel involved in calibration of equipment, sampling, and reading of measurements.

All records and test reports shall be safely stored, held secure and in confidence to the client and the competent authority, unless otherwise required by law.

5.4.5 *Handling of test samples or items*

A system for identifying the samples or materials to be tested shall be applied, either through documents or through marking, to ensure that there can be no confusion regarding the identity of the samples or items and the results of the measurements made.

The system shall include arrangements to ensure that the samples or items can be handled anonymously, *e.g.* to other clients.
A procedure shall exist for bonded storage of samples or items where necessary.

At all stages of storing, handling and preparation for test, precautions shall be taken to prevent damage to the samples or test material, for example contamination or the application of stresses (temperature), which would invalidate the results of testing. Any relevant instructions provided with the samples or materials to be tested shall be observed.

There shall be clear rules for the receipt, retention and disposal of samples and test materials.

5.4.6 *Confidentiality and security*

The personnel of the testing facility shall be bound to observe professional secrecy with regard to all information gained in carrying out its tasks.

The testing facility shall observe terms and conditions to provide for confidentiality and security of its practices as required by the user of its services.

5.4.7 *Subcontracting*

Testing facilities shall themselves normally perform the testing which they contract to undertake. Where, exceptionally, a testing facility subcontracts any part of the testing, this work shall be placed with another testing facility complying with these requirements. The testing facility shall ensure and be able to demonstrate that its subcontractor is competent to perform the services in question and complies with the same criteria of competence as the testing facility in respect of the work being subcontracted. The testing facility shall advise the client of its intention to subcontract any portion of the testing to another party. The subcontractor shall be acceptable to the client.

The testing facility shall record and retain details of its investigation of the competence and the compliance with the requirements of these Principles of GEP of its subcontractors and maintain a register of all subcontracting.

6 Cooperation

6.1 *Cooperation with clients*

The testing laboratory shall afford the client or his representative cooperation to enable him to clarify the client's request and to monitor the performance of the testing facility in relation to the work to be performed. This cooperation shall include:

a) affording the client or his representative access to relevant areas of the testing facility, for the witnessing of tests performed for the client. It is understood that such access shall by no means come into conflict with rules of confidentiality of work for other clients and with safety; and

b) preparation, packaging and dispatch of test samples or materials needed by the client for verification purposes.

The testing facility shall have a defined complaint procedure. This shall be documented and made available on request.

6.2 *Cooperation with competent authority*

The testing facility shall afford the competent authority and its authorized officers such reasonable cooperation as is necessary, to enable the competent authority to monitor compliance with these requirements and other relevant obligations. This cooperation shall include:

a) affording authorized officers' access to relevant areas of the testing facility, for the witnessing of tests;

b) undertaking any reasonable checks to enable the competent authority to verify the testing capability of the testing facility;

c) providing access to and copies of all relevant documentation and records necessary to verify compliance with these requirements;

d) preparation, packaging and dispatch of test samples or items needed by the competent authority for verification purposes;

e) participation in any appropriate programme of proficiency testing or comparison testing that the competent authority may reasonably deem to be necessary;

f) permitting scrutiny by the competent authority of the results of the testing facility's own internal audits and where appropriate, proficiency tests; and

g) where requested, making available, prior to the commencement of a test, detailed information concerning it, including its location and the materials to be tested.

6.3 *Cooperation with other laboratories and with bodies producing standards and guidelines*

Testing facilities are encouraged to participate in the drawing up of national, European or international standards and guidelines in the area of testing, where appropriate.

Testing facilities are encouraged to take part in an exchange of information with other laboratories and facilities having test activities in the same technical field where appropriate. The object is to have uniform test procedures and guidelines and to improve the quality of testing where appropriate.

In order to maintain the accuracy required, regular comparison of test results by proficiency testing should be arranged where appropriate.

7 **Further duties of testing facilities**

Testing facilities shall:

a) before undertaking testing, ensure that the competent authority has issued necessary authorizations for trials purposes, unless the testing concerning is to be conducted in accordance with the terms and conditions of a valid trials permit;

b) ensure, where relevant, that testing is conducted in accordance with the conditions of the relevant authorization for trials purposes;

c) at all times comply with the requirements of these Principles of GEP and with other criteria prescribed by the competent authority;

d) an annual report to the competent authority, containing all detailed information necessary to demonstrate compliance with these Principles of GEP;

e) claim that the Principles of Good Efficacy Testing Practice have been complied with only in respect of testing services that are carried out in accordance with the requirements of this Schedule and other criteria prescribed by the competent authority;

f) not use its compliance with this Schedule in such a manner as to bring the competent authority into disrepute and not make any statement relevant to compliance or non-compliance that the competent authority may reasonably consider to be misleading;

g) make it clear in all contracts with its clients that compliance with the Principles of Good Efficacy Testing Practice or test reports generated in accordance with those principles, by themselves in no way constitute or imply product authorization or approval by the competent authority or any other body;

h) ensure that no test report nor any part thereof shall be used by them, or be authorized for use by them, for promotional or publicity purposes, if the competent authority considers such use to be misleading; and

i) inform immediately the competent authority of any changes bearing on its compliance with the requirements of this Schedule and other criteria affecting the testing facility's capability or scope of activity.

Appendix 17

Regulations 25 (5)

DATA AND INFORMATION REQUIRED IN SUPPORT OF APPLICATIONS FOR AUTHORIZATION FOR TRIALS PURPOSES

INTRODUCTION

1 Although the extent of the data and information required to support applications for the authorization of plant protection products for trials purposes is quite limited, the tests and studies reported must satisfy the same standards as to quality, as is required of tests and studies submitted in support of applications for authorization for commercial marketing and use.

2 The information submitted must -

- include a technical dossier supplying the information necessary for evaluating the foreseeable immediate risks which the plant protection product may entail for humans, animals and the environment, as well as the information necessary for the identification of potential delayed risks for consumers through dietary exposure, and contain at least the information and results of the studies referred to below,
- comply with the relevant requirements specified in Annex II or Annex III.

3 The information provided must include the proposed classification of the plant protection product in accordance with the Regulations of 2001, its proposed labelling in accordance with these Regulations, as well as the classification and labelling or the proposed classification and labelling of each active substances contained in the plant protection product.

4 The information required must include a summary and overview of the information and study reports submitted. Where particular information, test reports or studies specified are not provided, the omission must be justified and a reasoned case must be made justifying the granting of an authorization for trials purposes, in the absence of the data concerned. Additional data, not specified hereunder, can be provided in support of applications, where it is of suitable quality, and relates to the risks that the plant protection product may entail for humans, animals and the environment.

5 Authorizations for trials purposes may not be granted where there are significant gaps in the supporting documentation provided. Decisions as to whether an authorization for trials purposes can be granted where there are minor gaps in the supporting documentation provided, can only be made on a case by case basis. The following general guidance is provided -

- in all cases at least that information and data specified hereunder concerning the identity of each active substance, the physical and chemical properties of each active substance, the identity of the plant protection product, the physical and chemical properties of the plant protection product and the acute toxicity of each active substance, must be provided; and
- where the nature of the proposed use is such that a there is a moderate or high risk of residues occurring in food or feed commodities, and where it is not proposed that produce be destroyed, data relating to the short-term toxicity and genotoxicity profile of each active substance, and data on residues at harvest, must be provided.

PART A

Chemical preparations

1 **Identity of the applicant**

The name and address of the applicant (permanent Community address) must be provided as must the name, position, telephone and telefax number of the appropriate person to contact.

Where, in addition, the applicant has an office, agent or representative within the territory of the State, the name and address of the local office, agent or representative must be provided as must the name, position, telephone and telefax number of the appropriate person to contact.

2 **Identity of the active substance(s)**

The information provided must be sufficient, to identify with precision each active substance in the plant protection product, to define it in terms of its specification and to characterize it as to its nature. The information and data referred to, unless otherwise specified, are required for all active substances.

2.1 *Common name proposed or ISO-accepted, and synonyms*

For each active substance in the plant protection product, the ISO common name, or proposed ISO common name, and where relevant, other proposed or accepted common names (synonyms), including the name (title) of the nomenclature authority concerned, must be provided.

2.2 *Chemical name (IUPAC and CA nomenclature)*

For each active substance in the plant protection product, the chemical name as given in Annex I to the Directive of 1967, or if not included in that Directive, in accordance with both IUPAC and CA nomenclature, must be provided.

2.3 *Manufacturer's development code number(s)*

For each active substance in the plant protection product, code numbers used to identify the active substances concerned and, where available, to identify formulations containing each of the active substances during development work, must be reported. For each code number reported, the material to which it relates, the period for which it was used, and the Member States or other countries in which it was used, and is being used, must be reported.

2.4 *CAS and EEC numbers (if available)*

For each active substance in the plant protection product, the Chemical Abstracts, EEC (EINECS or ELINCS), and CIPAC numbers, where they exist, must be reported.

2.5 *Molecular and structural formula, molecular mass*

The molecular formula, molecular mass and structural formula of each active substance, and where relevant, the structural formula of each stereo and optical isomer present in the active substances concerned, must be provided.

2.6 *Manufacturer (name, address, including location of plant)*

The name and address of the manufacturer or manufacturers of each active substance must be provided as must the name and address of each manufacturing plant in which the active substances concerned are manufactured. A contact point (preferably a central contact point, to include name, telephone and telefax number) must be provided, with a view to providing updating information and responding to queries arising, regarding manufacturing technology, processes and the quality of technical product (including where relevant, individual batches). Where following authorization for trials purposes, there are changes in the location or number of manufacturers, the information required must again be provided, unless the period of validity of the relevant authorization for trials purposes has expired or it has not been renewed.

2.7 *Specification of purity of active substance in g/kg or g/l as appropriate*

For each active substance in the plant protection product, the minimum content in g/kg of the pure active substance (excluding inactive isomers) in the manufactured material used in production of the formulated product, must be reported.

Where the information provided relates to a laboratory or pilot plant production system, the information required must again be provided once industrial scale production methods and procedures have stabilized, if production changes result in a changed specification of purity, unless the period of validity of the relevant authorization for trials purposes has expired or it has not been renewed.

3. **Physical and chemical properties of the active substance(s)**

3.1 *Melting point and boiling point*

3.1.1 The melting point or where appropriate the freezing or solidification point of purified active substance must be determined and reported according to EEC Method A 1. Measurements should be taken at temperatures up to 360 °C.

3.1.2 Where appropriate, the boiling point of purified active substances must be determined and reported according to EEC Method A 2. Measurements should be taken at temperatures up to 360 °C.

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

3.2 *Vapour pressure (in Pa) at 20?C, volatility (e.g. Henry's law constant)*

3.2.1 The vapour pressure of purified active substance, determined in accordance with EEC Method A 4, must be reported. Where vapour pressure is less than 10^{-5} Pa, the vapour pressure at 20 °C or 25 °C may be estimated, using a vapour pressure curve.

3.2.2 In the case of active substances that are solids or liquids, volatility (Henry's law constant) of purified active substance must be calculated from its water solubility and vapour pressure and be reported (in Pa x m^3 x mol^{-1}).

3.3 *Appearance (physical state, colour and odour; if known)*

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

3.3.2 A description of any odour associated with the active substance as manufactured and of purified active substance, noted when handling the materials in laboratories or production plants, must be reported.

3.4 *Solubility in water including effect of pH (4 to 10) on solubility*

The water solubility of purified active substances under atmospheric pressure, must be determined in accordance with EEC Method A 6, and be reported. These water solubility determinations must be made in the neutral range (*i.e.* in purified water in equilibrium with atmospheric carbon dioxide). Where the active substance is capable of forming ions, determinations must also be made in the acidic range (pH 4 to 6) and in the alkaline range (pH 8 to 10), and be reported. Where the stability of the active substance in aqueous media is such that water solubility cannot be determined, a justification based on test data must be provided.

3.5 *Solubility in organic solvents*

The solubility of active substances, as manufactured, in the following organic solvents at 15 to 25 °C must be determined and reported - if less than 250 g/kg, the temperature applied must be reported:

aliphatic hydrocarbon	- preferably n-heptane
aromatic hydrocarbon	- preferably xylene
halogenated hydrocarbon	- preferably 1,2-dichloroethane
alcohol	- preferably methanol or isopropyl alcohol
ketone	- preferably acetone
ester	- preferably ethyl acetate

If for a particular active substance, one or more of these solvents is unsuitable (*e.g.* reacts with test material), alternative solvents can be used instead. In such cases, choices made must be justified in terms of their structure and polarity.

3.6 *Partition coefficient n-octanol/water including effect of pH (4 to 10)*

The n-octanol/water partition coefficient of purified active substance must be determined and reported according to EEC Method A 8. The effect of pH (4 to 10) must be investigated when the substance is acidic or basic as defined by its pKa value (< 12 for acids, > 2 for bases).

3.7 *Flammability including auto-flammability*

3.7.1 The flammability of active substances as manufactured, which are solids, gasses, or are substances which evolve highly flammable gasses, must be determined in accordance with EEC Methods A 10, A 11, or A 12, as appropriate, and be reported.

3.7.2 The auto-flammability of active substances as manufactured must be determined in accordance with EEC Method A 15 or A 16, as appropriate, and/or, where necessary, according to the UN-Bowes-Cameron-Cage-Test (UN-Recommendations on the Transport of Dangerous Goods, Chapter 14, Nr. 14.3.4), and be reported.

3.8 *Flash point*

The flash point of active substances as manufactured, which have a melting point below 40 °C, must be determined in accordance with EEC Method A 9 and be reported; only closed cup methods should be used.

3.9 *Explosive properties*

The explosive properties of active substances as manufactured, must be determined in accordance with EEC Method A 14, where appropriate and be reported.

3.10 *Oxidizing properties*

The oxidizing properties of active substances as manufactured, must be determined in accordance with EEC Method A 17 and be reported, except where examination of their structural formulae, establishes beyond reasonable doubt that the active substance concerned is incapable of reacting exothermically with a combustible material. In such cases, it is sufficient to provide that information as justification for not determining the oxidizing properties of the substance.

4 Identity of the plant protection product

4.1 *Manufacturer of the preparation and the active substance(s) (names and addresses, etc. including location of plants)*

4.1.1 The name and address of the manufacturer of the preparation must be provided as must the name and address of each manufacturing plant in which the preparation is manufactured.

A contact point (preferably a central contact point, to include name, telephone and telefax numbers) must be provided for each.

4.2 *Trade name or proposed trade name, and manufacturer's development code number of the preparation if appropriate*

All former and current trade names and proposed trade names and development code numbers of the preparation as well as current names and numbers must be provided. Where trade names and code numbers referred to, relate to similar but different preparations (possibly obsolete), full details of the differences, must be provided.

4.3 *Detailed quantitative and qualitative information on the composition of the preparation (active substance(s), impurities, adjuvants, inert components, etc.)*

4.3.1 The following information must be reported -

- the content of both technical active substance(s) and pure active substance(s); and
- the content of formulants.

The concentrations must be expressed -

- for preparations that are solids, aerosols, volatile liquids (maximum boiling point 50 °C) or viscous liquids (lower limit 1 PA at 20 °C), as a percentage by weight,
- for other liquids, as a percentage by weight and in grams per litre at 20 °C, and
- for gasses, as a percentage by volume.

4.3.2 Formulants must where possible, be identified both by their chemical name as given in Annex I to the Directive of 1967, or, if not included in that Directive, in accordance with both IUPAC and CA nomenclature. Their structure or structural formula must be provided. For each component of formulants the relevant EEC (EINECS or ELINCS) number and CAS number where they exist, must be provided. Where the information provided does not fully identify a formulant, an appropriate specification must be provided. The trade name of formulants, where they exist, must also be provided.

4.3.3 For formulants the function must be given:

adhesive (sticker)	dye	repellent
antifoaming agent	emetic	safener
antifreeze	emulsifier	solvent
binder	fertilizer	stabiliser
buffer	preservative	synergist
carrier	odorant	thickener

deodorant	perfume	wetting agent
dispersing agent	propellant	miscellaneous (specify)

4.4 *Physical state and nature of the preparation (emulsifiable concentrate, wettable powder, solution etc.)*

The type and code of preparation must be designated in accordance with the "Catalogue of pesticide formulation types and international coding system (GIFAP Technical Monograph No 2 1989)".

Where a particular preparation is not defined precisely in that publication, a full description of the physical nature and state of the preparation must be provided, together with a proposal for a suitable description of the type of preparation and a proposal for its definition.

4.5 *Function (herbicide, insecticide, etc.)*

The function must be specified from among the following:

acaricide	molluscicide	semio-chemicals
bactericide	nematicide	talpicide
fungicide	plant growth regulator	viricide
herbicide	repellent	other (must be specified)
insecticide	rodenticide	

5 Physical and chemical properties of the plant protection product

5.1 *Appearance (physical state, colour and odour)*

A description of both the colour and odour, if any, and the physical state of the preparation, must be provided.

5.2 *Explosivity and oxidizing properties*

5.2.1 The explosive properties of preparations must be determined in accordance with EEC Method A 14 and be reported. Where available thermodynamic information establishes beyond reasonable doubt, that the preparation is incapable of exothermic reaction, it is sufficient to provide that information as a justification for not determining the explosive properties of the preparation.

5.2.2 The oxidizing properties of preparations that are solids, must be determined in accordance with EEC Method A 17 and be reported. For other preparations the method used must be justified. Oxidizing properties do not have to be determined if it can be shown without reasonable doubt, on the basis of thermodynamic information, that the preparation is incapable of reacting exothermically with combustible materials.

5.3 *Flash point and other indications of flammability or spontaneous ignition*

The flash point of liquids that contain flammable solvents, must be determined in accordance with EEC Method A 9 and be reported. The flammability of solid preparations and gasses must be determined in accordance with EEC Method A 10, A 11 or A 12, as appropriate, and be reported. The auto-flammability of preparations, determined in accordance with EEC Method A 15 or A 16 as appropriate, and/or, where necessary, in accordance with the UN-Bowes-Cameron-Cage-Test (UN-Recommendations on the Transport of Dangerous Goods, Chapter 14, Nr.14.3.4), must be reported.

5.4 *Acidity/alkalinity and if necessary pH value*

5.4.1 In the case of preparations that are acidic (pH < 4) or alkaline (pH > 10) the acidity or alkalinity and the pH value must be determined in accordance with CIPAC Method MT 31 and MT 75 respectively, and be reported.

5.4.2 Where relevant (if to be applied as aqueous dilution) the pH of a 1 % aqueous dilution, emulsion or dispersion of the preparation, must be determined in accordance with CIPAC Method MT 75 and be reported.

5.5 *Reactivity towards container materials*

The resistance of the proposed packaging material to its contents must be determined and reported.

6 Information on the proposed experimental use

6.1 *Field of use envisaged, e.g. field, protected crops, storage of plant products, home gardening*

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

Field use
- Agriculture
- Horticulture
- Forestry
- Viticulture

Protected crops

Amenity

Weed control on non-cultivated areas

Home gardening

House plants

Plant products storage practice

Other (specify)

6.2 *Effects on harmful organisms, e.g. contact, inhalation or stomach poison, fungitoxic or fungistatic, etc., systemic or not in plants*

6.2.1 The nature of the effects on harmful organisms must be stated:

contact action fungitoxic action reproduction inhibitor

stomach action fungistatic action other (must be specified)

inhalation actiondesiccant

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

6.3 *Details of intended use e.g. types of harmful organisms controlled and/or plants or plant products to be protected*

Details of the intended use must be provided.

Where relevant, effects achieved *e.g.* sprout suppression, retardation of ripening, reduction in stem length, enhanced fertilization *etc.* must be reported.

6.4 *Application rate*

For each method of application and each use, the maximum rate of application per unit (ha, m^2, m^3) treated, in terms of g or kg of both preparation and active substance, must be provided.

Application rates shall normally be expressed in g or kg/ha or in kg/m^3 and where appropriate in g or kg/tonne; for protected crops and home gardening use, rates shall be expressed in g or kg/100 m^2 or g or kg/m^3.

6.5 *Concentration of active substance in material used (e.g. in the diluted spray, baits or treated seed)*

The content of active substance shall be reported, as appropriate, in g/l, g/kg, mg/kg or in g/tonne.

6.6 *Method of application*

The method of application proposed must be described fully, indicating the type of equipment to be used, if any, as well as the type and volume of diluent to be used per unit of area or volume.

6.7 *Number and timing of applications and duration of protection*

The maximum number of applications to be used and their timing, must be reported. Where relevant the growth stages of the crop or plants to be protected and the development stages of the harmful organisms, must be indicated. Where possible the interval between applications, in days, must be stated.

The anticipated duration of protection afforded both by each application and by the maximum number of applications to be used, must be indicated.

6.8 *Necessary waiting periods or other precautions to avoid Phytotoxic effects on succeeding crops*

Where relevant, minimum waiting periods between last application and sowing or planting of succeeding crops, which are necessary to avoid phytotoxic effects on succeeding crops, must be stated.

Limitations on choice of succeeding crops, if any, must be stated.

6.9 *Proposed instructions for use*

The proposed instructions for use of the preparation, to be printed on labels and leaflets, must be provided.

7 Analytical methods

Where use is on a crop or plant product intended for use as food or feed, if residues may occur (moderate or high risk) and the crop or plant product is not to be destroyed, relevant, analytical methods including recovery rates and the limits of determination for residues in treated plants, plant products, foodstuffs and feeding-stuffs, must be provided.

8 Toxicological studies

8.1 *Acute toxicity*

8.1.1 *Oral*

8.1.1.1 The acute oral toxicity to the rat of each active substance in the preparation, determined in accordance with the EEC Method B 1 (Fixed Dose Method), must be reported.

8.1.1.2 The acute oral toxicity to the rat of the preparation, determined in accordance with the EEC Method B 1 (Fixed Dose Method), must be reported, except where, relevant information and documentation is submitted, or is available to the competent authority, which shows that there are valid grounds for assuming that classification resulting from calculation would not vary substantially from that obtainable by biological testing *i.e.* the composition of the preparation is

similar to that of a preparation for which a biological test is available, and the toxicity of the tested preparation is similar to its predicted toxicity, or the composition of the preparation is similar to that of two or more preparations for which biological tests are available, and the toxicity of the tested preparations varies in a consistent manner from their predicted toxicities.

8.1.2 *Percutaneous*

8.1.2.1 The acute percutaneous toxicity to rats of each active substance in the preparation, determined in accordance with EEC Method B 3, must be reported. Both local and systemic effects must be investigated.

8.1.2.2 The acute percutaneous toxicity to rats of the preparation, determined in accordance with EEC Method B 3, must be reported. Both local and systemic effects must be investigated. However, testing of the preparation should not be carried out, where relevant information and documentation is submitted, or is available to the competent authority, which shows that there are valid grounds for assuming that classification resulting from calculation would not vary substantially from that obtainable by biological testing *i.e.* the composition of the preparation is similar to that of a preparation for which a biological test is available, and the toxicity of the tested preparation is similar to its predicted toxicity, or the composition of the preparation is similar to that of two or more preparations for which biological tests are available, and the toxicity of the tested preparations varies in a consistent manner from their predicted toxicities.

8.1.3 *Inhalation*

8.1.3.1 The inhalation toxicity (EEC Method B 2) of the active substance must be reported where the active substance is -

- a gas or a liquefied gas,
- to be used as a fumigant,
- to be included in a smoke generating, aerosol or vapour releasing, preparation,
- to be used with fogging equipment,
- has a vapour pressure > 1 x 10^{-2} Pa and is to be included in preparations to be used in enclosed spaces such as warehouses or glasshouses,
- to be included in preparations which are powders containing a significant proportion of particles of diameter < 50 μm (> 1 % on a weight basis), or
- to be included in preparations to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 μm (> 1 % on a weight basis).

8.1.3.2 The inhalation toxicity (EEC Method B 2) of the plant protection product must be reported where it -

- is a gas or a liquefied gas,
- is a smoke generating formulation or a fumigant,
- is used with fogging equipment,
- is a vapour releasing preparation,
- is an aerosol,

- is a powder containing a significant proportion of particles of diameter < 50 µm (> 1 % on a weight basis),
- is to be applied from aircraft in cases where inhalation exposure is relevant,
- contains an active substance with a vapour pressure > 1 x 10^{-2} Pa and is to be used in enclosed spaces such as warehouses or glasshouses,
- is to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 µm (> 1 % on a weight basis).

However, testing of the preparation should not be carried out, where relevant information and documentation is submitted, or is available to the competent authority, which shows that there are valid grounds for assuming that classification resulting from calculation would not vary substantially from that obtainable by biological testing *i.e.* the composition of the preparation is similar to that of a preparation for which a biological test is available, and the toxicity of the tested preparation is similar to its predicted toxicity, or the composition of the preparation is similar to that of two or more preparations for which biological tests are available, and the toxicity of the tested preparations varies in a consistent manner from their predicted toxicities.

8.1.4 *Skin and where appropriate eye irritation*

8.1.4.1 The skin irritancy of each active substance, and of the preparation, determined using a single application to intact skin of rabbits, in accordance with EEC Method B 4, must be reported, except, where it is likely that severe skin effects may be produced, as indicated in the test guideline, or that effects can be excluded.

8.1.4.2 Eye irritation testing in accordance with EEC Method B 5 must be conducted for each active substances and the preparation, except where it is likely that severe effects on the eye may be produced, as indicated in the test guideline.

8.1.5 *Skin sensitisation*

8.1.5.1 Except where it is a known sensitizer, the potential of each active substance in the preparation, to provoke skin sensitisation reactions, must be assessed in accordance with the EEC Method B 6, using the Guinea-pig Maximization Test (GPMT), and be reported.

8.1.5.2 The potential of preparations to provoke skin sensitisation reactions, must be assessed in accordance with the EEC Method B 6, and be reported, except where the active substance(s) or co-formulants are known to have sensitising properties.

8.2 *Short-term toxicity of active substances*

8.2.1 *Oral 28-day study*

Circumstances in which required

Although it is not mandatory to perform 28-day short-term studies, they can be useful as range finding tests. Where conducted they must be reported, since the results can be of particular value in the identification of adaptive responses which can be masked in chronic toxicity studies.

Test Guideline

The test must be carried out in accordance with EEC Method B 7.

8.2.2 *Oral 90-day study*

Circumstances in which required

The short-term (90 day) of the active substance to both rat and dog, must always be reported. Where there is evidence that the dog is significantly more sensitive and where such data are likely to be of value in extrapolating results obtained to man, a 12-month toxicity study in dogs must be conducted and reported.

Test Guideline

Commission Directive 88/302/EEC, Part B, sub-chronic oral toxicity test.

8.3 *Genotoxicity testing*

Aim of the test

These studies are of value in -

- the prediction of genotoxic potential,
- the early identification of genotoxic carcinogens, and
- the elucidation of the mechanism of action of some carcinogens.

To avoid responses that are artefacts of the test system, excessively toxic doses must not be used in either *in vitro* or *in vivo* assays for mutagenicity. This approach should be regarded as general guidance. It is important that a flexible approach is adopted, with selection of further tests being dependant upon the interpretation of results obtained at each stage.

8.3.1 *In vitro studies*

Circumstances in which required

In vitro mutagenicity tests (bacterial assay for gene mutation, test for clastogenicity in mammalian cells and test for gene mutation in mammalian cells) must always be reported.

Test Guidelines

Acceptable test guidelines are -

- EEC Method B 14 - *Salmonella Typhimurium* reverse mutation assay,
- EEC Method B 10 - *in vitro* mammalian cytogenetic test,
- Commission Directive 88/302/EEC, Part B - *in vitro* mammalian cell gene mutation test.

8.3.2 *In vivo studies in somatic cells*

Circumstances in which required

If all the results of the *in vitro* studies are negative further testing must be done, taking into consideration all other relevant information available (including toxicokinetic, toxicodynamic and physico-chemical data and data on analogous substances). The test can be an *in vivo* study or an *in vitro* study using a different metabolising system from that/those previously used.

If the *in vitro* cytogenetic test is positive, an *in vitro* test using somatic cells (metaphase analysis in rodent bone marrow or micronucleus test in rodents) must be conducted.

If either of the *in vitro* gene mutation tests is positive, an *in vivo* test to investigate unscheduled DNA synthesis or a mouse spot test must be conducted.

Test Guidelines

Acceptable test guidelines are -

- EEC Method B 12 - micronucleus test,
- Commission Directive 88/302/EEC, Part B - mouse spot test,
- EEC Method B 11 - *in vivo* mammalian bone-marrow cytogenetic test, chromosomal analysis

8.3.3 *In vivo studies in germ cells*

Circumstances in which required

When any result of an *in vivo* study in somatic cells is positive, *in vitro* testing for germ cell effects may be justified. The necessity for conducting these tests will have to be considered on a case by case basis, taking into account information regarding toxicokinetics, use and anticipated exposure. Suitable tests involve interaction with DNA (such as the dominant lethal assay), to assess the potential for inherited effects and possibly to make a quantifiable assessment of heritable effects. It is recognized that in view of their complexity, the use of quantitative studies requires strong justification.

9 Residues in or on treated products, food or feed

9.1 *Nature of the residue*

A statement must be provided relating to the:

(i) identification of breakdown and reaction products and of metabolites in treated plants or plant products;

(ii) identification of breakdown and reaction products and of metabolites in succeeding crops, where relevant;

(iii) overall material balance for each active substance;

(iv) effects of industrial processing and/or household preparation on the nature and magnitude of residues, where relevant;

(v) results of feeding and metabolism studies in livestock (if residues remain in or on crops or parts of crops used for feed) to permit evaluation of residues in foodstuffs of animal origin; and

(vi) definition of the residue - for each active substance.

9.2 *Residue levels in treated products, food or feed*

9.1.1 Where on the basis of the rules relating to *Comparability, extrapolation, group tolerances and data requirements*, as contained in the *Guidelines for the generation of data concerning residues*, the residue levels likely to occur can be estimated on the basis of comparability,

- the rational and figures used,
- details of the GAPs used as a basis for the comparison, and
- detailed residue data, in summary form, for the crops with which the comparison is made,

must be provided.

9.1.2 In all other cases, sufficient residue data from supervised trials in crops, or plant products, for which authorization for trials purposes is sought, must be provided, giving all experimental conditions and details, including residue data concerning the active substance, relevant metabolites, degradation and reaction products, from time of application until harvest, or in the

case of post-harvest treatment, breakdown of residues during storage and levels of residues at time of release from storage for marketing.

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PART B

Preparations of micro-organisms

1 **Applicant**

The name and address of the applicant (permanent community address) must be provided, as must the name, position, telephone and telefax number of the appropriate person to contact.

Where, in addition, the applicant has an office, agent or representative in the territory of the State, the name and address of the local office, agent or representative must be provided, as must the name, position, telephone and telefax number of the appropriate person to contact.

2 **Producer**

The name and address of the producer or producers of the micro-organism must be provided as must the name and address of each plant in which the micro-organism is produced. A contact point (preferably a central contact point, to include name, telephone and telefax number) must be provided, with a view to providing updating information and responding to queries arising, regarding production technology, processes and the quality of product (including where relevant, individual batches).

3 **Identity of the active substance(s)**

The information provided must be sufficient, to identify with precision each active substance in the plant protection product, to define it in terms of its specification and to characterize it as to its nature. The information and data referred to, unless otherwise specified, are required for all active substances.

3.1 *Name and species description, strain characterization*

(i) The micro-organism must be deposited at an internationally recognized culture collection and have been given an accession number, details of which must be submitted.

(ii) Each micro-organism that is subject of an application must be identified and named at the species level. The scientific name and taxonomic grouping, *i.e.* family, genus, species, strain, serotype, pathovar or any other denomination relevant to the micro-organism, must be stated.

In relation to the micro-organism, an indication must be provided as to -

- whether it is indigenous or non-indigenous at the species level to the intended area of application,
- it is a wild type,
- it is a spontaneous or induced mutant, or
- it has been modified, using techniques described in Annex IA Part 2 and Annex IB of Directive 90/220/EEC.

In the latter 2 cases, all known differences between the modified micro-organism and the parent wild strain must be provided.

(iii) Best available technology must be used to identify and characterize the micro-organism at the strain level. The appropriate test procedures and criteria used for identification (*e.g.* morphology, biochemistry, serology, molecular identification) must be reported.

(iv) The common name or alternative and superseded names and code names used during the development, if any, must be provided.

(v) Relationships to known pathogens must be indicated

3.2 *Specification of the material used for manufacturing of formulated products*

3.2.1 *Content of the micro-organism*

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

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

Ideally the plant protection product should be free of contaminants (including contaminating micro-organisms). The acceptability of contaminants, their content and nature should be judged on the basis of a risk assessment conducted by the competent authority.

Where possible and appropriate, the identity and maximum content of all contaminating micro-organisms, expressed in appropriate units, must be reported. Information concerning identity must be provided where possible as specified in point 3.1.

Relevant metabolites (*i.e.* of concern from a human health and/or environmental perspective) formed by the micro-organism must be identified and characterized at different states or growth stages of the micro-organism.

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

In the case of chemical impurities that are relevant from a human health and/or the environmental perspective, their identity and maximum content, expressed in appropriate terms, must be provided.

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

Information on the identity of chemical substances such as additives must be provided in the form specified in point 1.10 of Part A of Annex II.

4 **Biological properties of the micro-organism**

4.1 *History of the micro-organism and its uses, natural occurrence and geographical distribution*

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

4.1.1 *Historical background*

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

4.1.2 *Origin and natural occurrence*

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

In the case of a mutant, or a genetically modified micro-organism (as defined in Annex IA Part 2 and Annex IB of Directive 90/220/EEC), detailed information must be provided on its production and isolation and on the means by which it can be clearly distinguished from the parent wild strain.

4.2 *Information on target organism(s)*

4.2.1 *Description of the target organism(s)*

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

4.2.2 *Mode of action*

The principal mode of action of the micro-organism must be indicated. Where relevant, it must be reported whether or not the micro-organism produces a toxin with a residual effect on the target organism. Where a toxin is produced, the mode of action of the toxin must be described.

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

The means by which uptake of the micro-organism, or its metabolites (especially toxins) may occur (*e.g.* contact, stomach, inhalation) must be described. It must also be indicated whether or not the micro-organism or its metabolites are translocated in plants and, where relevant, whether such translocation is apoplastic or symplastic or both.

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

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

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

Details of any experience of toxic effects of the active substance or its metabolic products on humans or animals must be reported. Available information indicating whether the organism is capable of colonizing or invading humans or animals (including immunosuppressed individuals) and whether it is pathogenic must be provided. Details must be provided of any experience concerning the active substance or its products indicating that it may irritate skin, eyes or respiratory organs of humans or animals or indicating that it is allergenic in contact with skin or when inhaled.

4.4 *Development stages / life cycle of the micro-organism*

Information must be presented in relation to the life cycle of the micro-organism, including information concerning symbiosis, parasitism, competitors, predators, host organisms, *etc.*, as well as vectors for viruses.

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

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

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

4.5 *Infectivity, dispersal and colonization ability*

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

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

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

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

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

4.6 *Relationships to known plant or animal or human pathogens*

The possible existence of one or more species of the genus of the active and/or, where relevant, contaminating micro-organisms known to be pathogenic to humans, animals, crops or other non-target species and the type of disease caused by them must be indicated. It must be reported whether or not it is possible, and if so, by which means the active micro-organism can be clearly distinguished from the pathogenic species.

4.7 *Genetic stability and factors affecting it*

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

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

4.8 *Information on the production of metabolites (especially toxins)*

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

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

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

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

4.9 *Antibiotics and other anti-microbial agents*

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

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

5 Identity of the plant protection product

5.1 *Manufacturer of the preparation*

The name and address of the manufacturer of the preparation must be provided as must the name and address of each manufacturing plant in which the preparation is manufactured.

A contact point (preferable a central contact point, to include name, telephone and telefax numbers) must be provided for each manufacturer.

5.2 *Trade name or proposed trade name, and manufacturer's development code number of the preparation if appropriate*

All former and current trade names and proposed trade names and development code numbers of the preparation as well as the current names and numbers must be provided. Where trade names and code numbers referred to, relate to similar but different preparations (possibly obsolete), full detail of the differences must be provided. (The proposed trade name may not give rise to confusion with the trade names of plant protection products already authorized.)

5.3 *Detailed quantitative and qualitative information on the composition of the preparation*

5.3.1 The following information must be reported -

- content of the micro-organism(s) in the plant protection product and the content of the micro-organism in the material used for manufacturing plant protection products. The maximum, minimum and nominal content of the viable and non-viable material must be provided,
- content of formulants,
- content of other components (*e.g.* by-products, condensates, culture medium, *etc.*) and contaminating micro-organisms, derived from the production process.

Concentrations must be expressed for chemicals -

- for preparations that are solids, aerosols, volatile liquids (maximum boiling point 50 °C) or viscous liquids (lower limit 1 PA at 20 °C), as a percentage by weight,
- for other liquids, as a percentage by weight and in grams per litre at 20 °C, and
- for gasses, as a percentage by volume, and

in the case of micro-organisms in other appropriate terms (*e.g.* number of active units per volume or weight or other manner appropriate for micro-organisms).

5.3.2 Formulants must where possible, be identified either by their chemical name as given in Annex I to the Directive of 1967, or, if not included in that Directive, in accordance with both IUPAC and CA nomenclature. Their structure or structural formula must be provided. For each component of formulants the relevant EEC (EINECS or ELINCS) number and CAS number where they exist, must be provided. Where the information provided does not fully identify a formulant, an appropriate specification must be provided. The trade name of formulants, where they exist, must also be provided.

5.3.3 For formulants their function must be given -

adhesive (sticker)	dye	repellent
antifoaming agent	emetic	safener
antifreeze	emulsifier	solvent
binder	fertilizer	stabiliser
buffer	odorant	synergist
carrier	perfume	thickener
deodorant	preservative	wetting agent
dispersing agent	propellant	miscellaneous (specify)

5.3.4 The identify of contaminating micro-organisms and other components derived from production process must be provided.

5.4 *Physical state and nature of the preparation*

The type and code of the preparation must be designated according to the "Catalogue of pesticide formulation types and international coding system (GIFAP Technical Monograph No 2, 1989)"

Where a particular preparation is not defined precisely in that publication a full description of the physical nature and state of the preparation must be provided, together with a proposal for a suitable description of the type of preparation and a proposal for its definition.

5.5 ***Function***

The biological function of the preparation must be specified from among the following -

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

6 **Physical, chemical and technical properties of the plant protection product**

6.1 *Appearance (colour and odour)*

A description of both the colour and odour, if any, and the physical state of the preparation, must be provided.

6.2 *Explosivity and oxidizing properties*

6.3.1 The explosive properties of preparations must be determined in accordance with EEC Method A 14 and be reported. Where available thermodynamic information establishes beyond reasonable doubt, that the preparation is incapable of exothermic reaction, it is sufficient to provide that information as a justification for not determining the explosive properties of the preparation.

6.3.2 The oxidizing properties of preparations that are solids, must be determined in accordance with EEC Method A 17 and be reported. For other preparations the method used must be justified. Oxidizing properties do not have to be determined if it can be shown without reasonable doubt, on the basis of thermodynamic information, that the preparation is incapable of reacting exothermically with combustible materials.

6.4 *Flash point and other indications of flammability or spontaneous ignition*

Flash point and flammability must be determined and be reported, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

The flash point of liquids that contain flammable solvents, must be determined in accordance with EEC Method A 9 and be reported. The flammability of solid preparations and gasses must be determined in accordance with EEC Method A 10, A 11 or A 12, as appropriate, and be reported. The auto-flammability of preparations, determined in accordance with EEC

Method A 15 or A 16 as appropriate, and/or, where necessary, in accordance with the UN-Bowes-Cameron-Cage-Test (UN-Recommendations on the Transport of Dangerous Goods, Chapter 14, Nr.14.3.4), must be reported.

6.5 *Acidity, alkalinity and if necessary pH value*

Acidity, alkalinity and pH must be determined and be reported unless it can be justified that it is technically or scientifically not necessary to perform such studies.

6.5.1 In the case of preparations that are acidic (pH < 4) or alkaline (pH > 10) the acidity or alkalinity and the pH value must be determined in accordance with CIPAC Method MT 31 and MT 75 respectively, and be reported.

6.5.2 Where relevant (if to be applied as aqueous dilution) the pH of a 1 % aqueous dilution, emulsion or dispersion of the preparation, must be determined in accordance with CIPAC Method MT 75 and be reported.

7 Information on the proposed experimental use

7.1 *Field of use envisaged*

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

Field use
- Agriculture
- Horticulture
- Forestry
- Viticulture

Protected crops

Amenity

Weed control on non-cultivated areas

Home gardening

House plants

Plant products storage practice

Other (specify)

7.2 *Effects on harmful organisms*

The mechanism by which uptake of the micro-organism, or its metabolites (especially toxins) occurs (*e.g.* contact, stomach, inhalation) must be described as must the type of controlling action (*e.g.* fungitoxic, fungistatic action, nutrient competition, *etc.*).

It must also be stated whether or not the product is translocated in plants and, where relevant, if such translocation is apoplastic, symplastic or both.

7.3 *Details of intended use*

Details of the intended use, *e.g.* types of harmful organisms controlled and/or plants or plant products to be protected, must be provided.

7.4 *Application rate*

For each method of application and each use, the rate of application per unit (ha, m^2, m^3) treated, in terms of g or kg or L for the preparation and in terms of appropriate units for the micro-organism, must be provided.

Application rates must normally be expressed in g or kg/ha or in kg/m^3 and where appropriate in g or kg/tonne; for protected crops and home gardening use, rates must be expressed in g or kg/100m^2 or g or kg/m^3.

7.5 *Content of micro-organism in material used (e.g. in the diluted spray, baits or treated seed)*

The content of micro-organism must be reported, as appropriate, in terms of number of active unit/ml or g or any other relevant unit.

7.6 *Method of application*

The method of application proposed must be described fully, indicating the type of equipment to be used, if any, as well as the type and volume of diluent to be used per unit of area or volume.

7.7 *Number and timing of applications and duration of protection*

The maximum number of applications to be used and their timing must be reported. Where relevant the growth stages of the crop or plants to be protected and the development stages of the harmful organisms, must be indicated. Where possible and necessary the interval between applications, in days, must be stated.

The duration of protection afforded both by each application and by the maximum number of applications to be used, must be indicated.

7.8 *Necessary waiting periods or other precautions to avoid phytopathogenic effects on succeeding crops*

Where relevant, minimum waiting periods between last application and sowing or planting of succeeding crops, that are necessary to avoid phytopathogenic effects on succeeding crops, must be stated.

Limitations on choice of succeeding crops, if any, must be stated.

7.9 *Proposed instructions for use*

The proposed instructions for use of the preparation, to be printed on labels and leaflets, must be provided.

8 Methods to determine and quantify residues

Where use is on a crop or plant product intended for use as food or feed, if residues may occur (moderate or high risk) and the crop or plant product is not to be destroyed, relevant, analytical methods including recovery rates and the limits of determination for residues in treated plants, plant products, foodstuffs and feeding-stuffs, must be provided in relation to -

- the active micro-organism(s), and
- relevant metabolites (especially toxins)

9 Effects on human health

9.1 *Sensitisation*

Except where it is known sensitizer, the potential of each micro-organism in the preparation to provoke sensitisation reactions by inhalation as well as following dermal exposure must be assessed. A maximization test must be performed.

9.2 *Acute toxicity, pathogenicity and infectivity*

9.2.1 The acute oral toxicity, pathogenicity and infectivity of the micro-organism in the preparation must be reported.

9.2.2 The acute oral toxicity, pathogenicity and infectivity of the preparation must be reported, unless relevant information and documentation is submitted, or is available to the competent authority, which shows that there are valid grounds for assuming that classification resulting from calculation would not vary substantially from that obtainable by biological testing *i.e.* the composition of the preparation is similar to that of a preparation for which a biological test is available, and the effects of the tested preparation are similar predicted, or the composition of the preparation is similar to that of two or more preparations for which biological tests are available, and the effects of the tested preparations vary in a consistent manner from those predicted.

9.3 *Acute inhalation toxicity, pathogenicity and infectivity*

9.3.1 The acute inhalation toxicity, pathogenicity and infectivity of the micro-organism in the preparation must be reported.

9.3.2 The acute inhalation toxicity, pathogenicity and infectivity of the preparation must be reported, unless relevant information and documentation is submitted, or is available to the competent authority, which shows that there are valid grounds for assuming that classification resulting from calculation would not vary substantially from that obtainable by biological testing *i.e.* the composition of the preparation is similar to that of a preparation for which a biological test is available, and the effects of the tested preparation are similar predicted, or the composition of the preparation is similar to that of two or more preparations for which biological tests are available, and the effects of the tested preparations vary in a consistent manner from those predicted.

9.4 *Intraperitoneal/Subcutaneous single dose*

An intraperitoneal/subcutaneous test is a highly sensitive assay to assess in particular infectivity. The intraperitoneal route is in principle required for all micro-organisms, however expert judgement may be exercised in deciding whether subcutaneous injection is preferred instead of intraperitoneal injection where the maximum temperature for growth and multiplication is lower than 37 °C.

9.5 *Cell culture study*

A cell culture study must be reported for intracellular replicating micro-organisms, such as viruses, viroids or specific bacteria and protozoa, unless available information provided clearly demonstrate that the micro-organism does not replicate in warm blooded organisms. The study should be performed using human cell or tissue cultures of different organs. Selection can be based on expected target organs following infection. Where human cell or tissue cultures of specific organs are not available, other mammalian cell and tissue cultures can be used. In the case of viruses, ability to interact with the human genome is a key consideration.

9.6 *Information on short-term toxicity and pathogenicity*

Aim of the test

Short-term toxicity studies must be designed to provide information as to the amount of the micro-organism that can be tolerated without toxic effects under the conditions of the study. Such studies provide useful data on the risks for those handling and using preparations containing the micro-organism. In particular, short-term studies provide an essential insight into possible cumulative effects of the micro-organism, and the risks to workers who may be exposed over extensive periods. In addition short-term studies provide information useful in the design of chronic toxicity studies.

The studies, data and information to be provided and evaluated, must be sufficient to permit the identification of effects following repeated exposure to the micro-organism, and in particular to further establish, or indicate -

- the relationship between dose and adverse effects,
- the toxicity of the micro-organism including where possible the NOAEL for toxins,
- the target organs, where relevant,
- the time course and characteristics of the effects with full details of behavioural changes and possible gross pathological findings at post-mortem,

- specific toxic effects and pathological changes produced,
- where relevant the persistence and reversibility of certain toxic effects observed, following discontinuation of dosing,
- where possible, the mode of toxic action, and
- the relative hazard associated with the different routes of exposure.

During short-term toxicity testing, an estimation must be made of the clearance of the micro-organism clearance in the main organs.

Pathogenicity and infectivity end points must be investigated and be reported

Circumstances in which required

The short-term toxicity (minimum 28 days) of the micro-organism must be reported.

The choice of test species must be justified. A decision concerning study duration should reflect acute toxicity and clearance data.

Expert judgement is required to decide the route of administration that is appropriate in individual cases.

9.7 *Health effects after repeated inhalation exposure*

Information on health effects following repeated exposure by the inhalation route is necessary, particularly for risk assessment in relation to occupational situations. Repeated exposure can influence the clearance capacity (*e.g.* resistance) of the host (human). Furthermore, toxicity following repeated exposure to contaminants, growth medium, co-formulants and the micro-organism must be addressed to facilitate proper risk assessment. It must be appreciated that formulants in the plant protection product can influence the toxicity and infectivity of a micro-organism.

Circumstances in which required.

Information on the short-term infectivity, pathogenicity and toxicity by the inhalation route is required, unless the information otherwise provided is sufficient to permit assessment of human health effects. This can be the case where it is demonstrated that the test material has no inhalable fraction and/or repeated exposure is not expected.

9.8 *Genotoxicity testing*

Circumstances in which required

If exotoxins are produced by the micro-organism, those exotoxins and any other relevant metabolites in the culture medium must be tested for genotoxicity. Where possible testing should be carried out using purified toxins and metabolites.

Where, on the basis of expert judgement and having regard to the relevance and validity of the data available, it is concluded that there is no evidence that toxic metabolites are formed, testing

on the micro-organism itself must be considered. In the case of viruses the risk of insertional mutagenesis in mammal cells or the risk of carcinogenicity must be considered.

Aim of the test

These studies are of value in -

- the prediction of genotoxic potential,
- the early identification of genotoxic carcinogens, and
- the elucidation of the mechanism of action of some carcinogens.

It is important that a flexible approach is adopted, with selection of further tests being dependent upon interpretation of results at each stage.

Test conditions

The genotoxicity potential of cellular micro-organisms should, whenever possible, be studied using broken cells. A justification must be provided as to the suitability of the method of sample preparation used

In the case of viruses infectious isolates must be used for testing.

9.8.1 *In vitro studies*

Circumstances in which required

In vitro mutagenicity tests (bacterial assay for gene mutation, test for clastogenicity in mammalian cells and test for gene mutation in mammalian cells) must be provided.

9.8.2 *In vivo studies in somatic cells*

Circumstances in which required

If all the results of the *in vitro* studies are negative further testing must be done, taking into consideration all other relevant information available (including toxicokinetic, toxicodynamic and physico-chemical data and data on analogous micro-organisms, toxins and metabolites). The test can be an *in vivo* study or an *in vitro* study using a different metabolising system from that/those previously used.

If the *in vitro* cytogenetic test is positive, an *in vivo* test using somatic cells (metaphase analysis in rodent bone marrow or micronucleus test in rodents) must be conducted.

If either of the *in vitro* gene mutation tests is positive, an *in vivo* test to investigate unscheduled DNA synthesis or a mouse spot test must be conducted.

9.8.3 *In vivo studies in germ cells*

Circumstances in which required

When any result of an *in vivo* study in somatic cells is positive, *in vivo* testing for germ cell effects may be justified. The necessity for conducting these tests will have to be considered on a case by case basis, taking into account information regarding toxicokinetics, use and anticipated exposure. Suitable tests involve interaction with DNA (such as the dominant lethal assay), to assess the potential for inherited effects and possibly make a quantitative assessment of heritable effects. It is recognised that in view of their complexity, the use of quantitative studies requires strong justification.

10 Residues in or on treated products, food or feed

10.1 *Nature of the residue*

A statement must be provided relating to the:

(i) identification of the micro-organisms (viable and non-viable), metabolites and toxins in treated plants or plant products;

(ii) identification of the micro-organisms (viable and non-viable), metabolites and toxins in succeeding crops, where relevant;

(iii) overall material balance for each active substance;

(iv) effects of industrial processing and/or household preparation on the nature and magnitude of residues, where relevant;

(v) results of feeding and metabolism studies in livestock (if residues remain in or on crops or parts of crops used for feed) to permit evaluation of residues in foodstuffs of animal origin; and

(vi) definition of the residue - for each active substance.

10.2 *Residue levels in treated products, food or feed*

10.1.1 Where on the basis of the rules relating to *Comparability, extrapolation, group tolerances and data requirements*, as contained in the *Guidelines for the generation of data concerning residues*, the residue levels likely to occur can be estimated on the basis of comparability,

- the rational and figures used,
- details of the GAPs used as a basis for the comparison, and
- detailed residue data, in summary form, for the crops with which the comparison is made,

must be provided.

10.1.2 In all other cases, sufficient residue data from supervised trials in crops, or plant products, for which authorization for trials purposes is sought, must be provided, giving all experimental conditions and details, including residue data concerning the active substance, relevant metabolites, degradation and reaction products, from time of application until harvest, or in the case of post-harvest treatment, breakdown of residues during storage and levels of residues at time of release from storage for marketing.

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Appendix 18

Regulation 30 (6) (d)

CERTIFICATE OF RESULT OF ANALYSIS

Laboratory Reference Number .....

Sample of .....

received by the designated chemist on .....

from .....

Methods of analysis used .....

.....

.....

.....

This is to certify that the above mentioned sample, which was duly fastened and sealed, has been analysed under the provisions of the European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) Regulations, 2002 (**S.I. No. xx of 2002**) and the results of the analysis are as follows:-

.....

.....

.....

.....

.....

This certificate is issued under the European Communities (Authorization, Placing on the Market, Use and Control of Plant Protection Products) Regulations, 2002 (**S.I. No. xx of 2002**).

Date .....

Signed .....
Designated Analyst.

.....
Designated Analyst.

.....
Designated Analyst.

Appendix 19

APPLICATION AND ANNUAL FEES FOR AUTHORIZATION OF PLANT PROTECTION PRODUCTS

PART 1

Regulations 34 (1) (a) and (c)

Fees for the consideration of applications for the authorization of plant protection products in accordance with Regulations 13, 15 and 18, and for their renewal in accordance with Regulation 19 (1)

Column (1)	Column (2)
Each Annex II A dossier as specified in Regulation 8 (3) (b)	€5,700
Each Annex II B dossier as specified in Regulation 8 (3) (b)	€ 250
Each Annex III A dossier as specified in Regulation 8 (3) (a)	€2,000
Each Annex III B dossier as specified in Regulation 8 (3) (a)	€ 250
Each dossier as specified in Regulation 8 (6) for preparations containing chemical active substance(s)	€1,625
Each dossier as specified in Regulation 8 (6) for preparations containing active substance(s) that are micro-organisms or viruses	€ 200

PART 2

Regulation 34 (1) (b)

Fees for the consideration of applications for the inclusion of an active substance in Annex I of the Directive, for the renewal of any such inclusion and for the modification of any conditions or restrictions associated with the inclusion of an active substance in Annex I

Column (1)	Column (2)
Receipt, registry and completeness check	€ 2,000
Data and information relating to identity, physical and chemical properties and methods of analysis	€13,300
Toxicological and metabolism data and information	€33,300
Data and information relating to residues	€26,600
Data and information relating to fate and behaviour in the environment	€26,600
Ecotoxicological data and information	€26,600
Co-ordination of evaluation and preparation of monograph	€13,300
Evaluation of further data and comments provided	€63,300

PART 3

Regulation 34 (1) (d)

Fees for the consideration of applications for modification of authorization for plant protection products in accordance with Regulation 19 (4)

Column (1) Category	Column (2)
I	€2,000
II	€ 750

"Category I" means a modification in the authorization of a plant protection product involving a major additional use, a major change in the manner of use, or a major formulation change;

"Category II" means a modification in the authorization of a plant protection product involving a minor additional use, a minor change in the manner of use, or a minor formulation change.

PART 4

Regulations 34 (4) (a), (b) and (f)

Annual Fees:	€275
Late Annual Fees:	€400

PART 5

Regulations 34 (5) and (6)

A. Reduced fees payable for plant protection products for specialized use or uses, already on the market for 3 calendar years

Column (1)	Column (2)
Wholesale sales in each of three calendar years immediately prior to the year in which the fee is payable	Percentage of the fee payable %
less than €6,500	10
€6,500 to €12,999	25
€13,000 to €25,999	50

B. Reduced fees payable for plant protection products for specialized use or uses, on the market for less than 3 calendar years

Column (1)	Column (2)
Estimated potential annual wholesale sales	Percentage of the fee payable %
less than €13,000	10
€13,000 to €25,999	25
€26,000 to €51,999	50