



Flusilazole
6850/VI/97 final
5 January 2007

Review report for the active substance **flusilazole**
finalised in the Standing Committee on Plant Health at its
meeting on 3 March 2006
in view of the inclusion of flusilazole in Annex I of Directive 91/414/EEC

1. Procedure followed for the re-evaluation process

This review report has been established as a result of the re-evaluation of flusilazole, made in the context of the work programme for review of existing active substances provided for in Article 8(2) of Directive 91/414/EEC concerning the placing of plant protection products on the market, with a view to the possible inclusion of this substance in Annex I to the Directive.

Commission Regulation (EEC) No 3600/92⁽¹⁾ laying down the detailed rules for the implementation of the first stage of the programme of work referred to in Article 8(2) of Council Directive 91/414/EEC, as last amended by Regulation (EC) No 1972/99⁽²⁾, has laid down the detailed rules on the procedure according to which the re-evaluation has to be carried out. flusilazole is one of the 90 existing active substances covered by this Regulation.

In accordance with the provisions of Article 4 of Regulation (EEC) No 3600/92, DuPont de Nemours on 23 July 1993 notified to the Commission of their wish to secure the inclusion of the active substance flusilazole in Annex I to the Directive.

In accordance with the provisions of Article 5 of Regulation (EEC) No 3600/92, the Commission, by its Regulation (EEC) No 933/94⁽³⁾, as last amended by Regulation (EC) No 2230/95⁽⁴⁾, designated Ireland as rapporteur Member State to carry out the assessment of flusilazole on the basis of the dossier submitted by the notifier. In the same Regulation, the Commission specified furthermore the deadline for the notifiers with regard to the submission to the rapporteur Member States of the dossiers required under Article 6(2) of Regulation (EEC) No 3600/92, as well as for other parties with regard to further technical and scientific information; for flusilazole this deadline was 30 April 1995.

DuPont de Nemours submitted a dossier to the rapporteur Member State which was considered as complete. Information has furthermore been submitted by third parties, including the

¹ OJ No L 366, 15.12.1992, p.10.

² OJ No L 244, 16.09.1999, p.41.

³ OJ No L 107, 28.04.1994, p.8.

⁴ OJ No L 225, 22.09.1995, p.1.

European Federation of Agricultural Workers' Unions (EFA), the European Environmental Bureau (EEB) and the European consumer associations COFACE, EURO COOP and EURO-C-ETUC. Furthermore evaluation documentation from KEMI, Sweden, and comments from Member States were considered.

In accordance with the provisions of Article 7(1) of Regulation (EEC) No 3600/92, Ireland submitted on 30 April 1996 to the Commission the report of its examination, hereafter referred to as the draft assessment report, including, as required, a recommendation concerning the possible inclusion of flusilazole in Annex I to the Directive. Moreover, in accordance with the same provisions, the Commission and the Member States received also the summary dossier on flusilazole from DuPont de Nemours on 26 August 1996.

In accordance with the provisions of Article 7(3) of Regulation (EEC) No 3600/92, the Commission forwarded for consultation the draft assessment report to all the Member States on 17 October 1996 as well as to DuPont de Nemours being the main data submitter, on 20 November 1996.

The Commission organised an intensive consultation of technical experts from a certain number of Member States, to review the draft assessment report and the comments received thereon (peer review), in particular on each of the following disciplines:

- identity and physical /chemical properties ;
- fate and behaviour in the environment ;
- ecotoxicology ;
- mammalian toxicology ;
- residues and analytical methods ;
- regulatory questions.

The meetings for this consultation were organised on behalf of the Commission by the Biologische Bundesanstalt für Land und Forstwirtschaft (BBA) in Braunschweig, Germany, from January to April 1997.

The report of the peer review (i.e. full report) was circulated, for further consultation, to Member States and the main data submitter on 14 April 1997 for comments and further clarification.

In accordance with the provisions of Article 6(4) of Directive 91/414/EEC concerning consultation in the light of a possible unfavourable decision for the active substance the Commission organised a tripartite meeting with the main data submitter and the rapporteur Member State for this active substance on 4 November 1997.

In accordance with the provisions of Article 7(3) of Regulation (EEC) No 3600/92, the dossier, the draft assessment report including an addendum, the peer review report (i.e. full report) and the comments and clarifications on the remaining issues, received after the peer review were referred to the Standing Committee on Plant Health, and specialised working groups of this Committee, for final examination, with participation of experts from the 15 Member States. This final examination took place from December 1997 to January 2001, and was finalised in the meeting of the Standing Committee on 3 March 2006.

As regards flusilazole two questions have been submitted to the Scientific Committee⁵. The first was whether the proposed NOEC for long term effect on fish was adequate to ensure a sufficient protection from adverse effects on reproduction and, more general, what is the position of the Committee concerning the comparative sensitivity of the early life stage test vs. the full fish life cycle study. The Committee concluded that fish early life-stage tests provide useful information but that they are not designed to detect potential effects on reproduction. Considering there is evidence that flusilazole may have specific effects on the reproductive process, it cannot conclude that a NOEC based on this test is necessarily adequate in this case. The conclusions of the Committee have been addressed through a full fish life cycle test; the evaluation within the Standing Committee concluded that the chronic risk is acceptable. The second question related to the potential impact on organic matter decomposition. Here, the Committee concluded that the tests, initially limited to earthworms and soil microflora, were not adequate to fully assess such impact. The conclusion has been duly taken into consideration and the additional litter bag test using the highest recommended dose rate and the ten-fold recommended dose rate provided have been considered to adequately address the question.

The present review report contains the conclusions of this final examination; given the importance of the draft assessment report, the peer review report (i.e. full report) and the comments and clarifications submitted after the peer review as basic information for the final examination process, these documents are considered respectively as background documents A, B and C to this review report and are part of it.

2. Purposes of this review report

This review report, including the background documents and appendices thereto, have been developed and finalised in support of the Directive 2006/133/EC concerning the inclusion of flusilazole in Annex I to Directive 91/414/EEC, and to assist the Member States in decisions on individual plant protection products containing flusilazole they have to take in accordance with the provisions of that Directive, and in particular the provisions of article 4(1) and the uniform principles laid down in Annex VI.

This review report provides also for the evaluation required under Section A.2.(b) of the above mentioned uniform principles, as well as under several specific sections of part B of these principles. In these sections it is provided that Member States, in evaluating applications and granting authorisations, shall take into account the information concerning the active substance in Annex II of the directive, submitted for the purpose of inclusion of the active substance in Annex I, as well as the result of the evaluation of those data.

In accordance with the provisions of Article 7(6) of Regulation (EEC) No 3600/92, Member States will keep available or make available this review report for consultation by any interested parties or will make it available to them on their specific request. Moreover the Commission will send a copy of this review report (not including the background documents) to all operators having notified for this active substance under Article 4(1) of this Regulation.

⁵ Opinion of the Scientific Committee on Plants on specific questions from the Commission concerning the evaluation of Flusilazole in the context of Council Directive 91/414/EEC (Opinion adopted by the Scientific Committee on Plants on 18 July 2002)

The information in this review report is, at least partly, based on information, which is confidential and/or protected under the provisions of Directive 91/414/EEC. It is therefore recommended that this review report would not be accepted to support any registration outside the context of Directive 91/414/EEC, e.g. in third countries, for which the applicant has not demonstrated to have regulatory access to the information on which this review report is based.

3. Overall conclusion in the context of Directive 91/414/EEC

The overall conclusion from the evaluation is that it may be expected that plant protection products containing flusilazole will fulfil the safety requirements laid down in Article 5(1)(a) and (b) of Directive 91/414/EEC. This conclusion is however subject to compliance with the particular requirements in sections 4, 5, 6 and 7 of this report, as well as to the implementation of the provisions of Article 4(1) and the uniform principles laid down in Annex VI of Directive 91/414/EEC, for each flusilazole containing plant protection product for which Member States will grant or review the authorisation.

Furthermore, these conclusions were reached within the framework of the following uses which were proposed and supported by the main data submitter:

- fungicide for use on cereals, maize, oilseed rape and sugarbeet

With particular regard to residues, the review has established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health. The International Estimated Daily Intake (IEDI) for a 60 kg adult is 72% of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994). Estimates of acute dietary exposure of adults and toddlers for the proposed uses do not exceed the Acute Reference Dose (ARfD). Additional intake from water is not expected to give rise to intake problems.

The review has identified acceptable exposure scenarios for operators, workers and bystanders, which require however to be confirmed for each plant protection product in accordance with the relevant sections of the above mentioned uniform principles.

The review has also concluded that under the proposed and supported conditions of use there are no unacceptable effects on the environment, as provided for in Article 4(1) (b) (iv) and (v) of Directive 91/414/EEC, provided that certain conditions are taken into account as detailed in section 6 of this report.

4. Identity and Physical/chemical properties

The main identity and the physical/chemical properties of flusilazole are given in Appendix I.

The active substance shall comply with the FAO specification and there seem not to be reasons for deviating from that specification; the FAO specification is given in Appendix I of this report.

The review has established that for the active substance notified by the main data submitter DuPont de Nemours none of the manufacturing impurities considered are, on the basis of information currently available, of toxicological or environmental concern.

5. Endpoints and related information

In order to facilitate Member States in the application of the provisions of Article 4(1) of Directive 91/414/EEC and the uniform principles laid down in Annex VI of that Directive for the purposes of granting or reviewing authorisations, the most important endpoints identified during the re-evaluation process referred to at point 1 above, are listed in Appendix II.

6. Particular conditions to be taken into account on short term basis by Member States in relation to the granting of authorisations of plant protection products containing flusilazole

On the basis of the proposed and supported uses, the following particular issues have been identified as requiring particular and short term attention from all Member States, in the framework of any authorisations to be granted, varied or withdrawn, as appropriate:

Therefore, Member States must apply risk mitigation measures and pay particular attention to the protection of:

- aquatic organisms and where relevant an appropriate distance must be kept between treated areas and surface water bodies.
- birds and mammals by providing judicious timing of the application and the selection of those formulations which, as a result of their physical presentation or the presence of agents that ensure an adequate avoidance, minimise the exposure of the concerned species;
- operators, who must wear suitable protective clothing during mixing, loading, application and cleaning of the equipment, unless the exposure to the substance is adequately precluded by the design and construction of the equipment itself or by the mounting of specific protective components on such equipment.

7. List of studies to be generated

No further studies were identified which were at this stage considered necessary in relation to the inclusion of flusilazole in Annex I under the current inclusion conditions.

However, further studies shall be requested by the Member States to address the potential endocrine disrupting properties of flusilazole within two years after the adoption of the Test Guidelines on endocrine disruption by the Organisation for Economic Cooperation and Development (OECD).

Member States must ensure that the authorisation holders report at the latest on 31 December of each year on incidences of operator health problems, may require sales data and a survey of use patterns so that a realistic picture of the use conditions and the possible toxicological impact of flusilazole can be obtained.

8. Information on studies with claimed data protection

For information of any interested parties, Appendix III gives information about the studies for which the main data submitter has claimed data protection and which during the re-evaluation process were considered as essential with a view to Annex I inclusion. This information is only given to facilitate the operation of the provisions of Article 13 of Directive 91/414/EEC in the Member States. It is based on the best information available to the Commission services at the time this review report was prepared; but it does not prejudice any rights or obligations of Member States or operators with regard to its uses in the implementation of the provisions of Article 13 of the Directive 91/414/EEC neither does it commit the Commission.

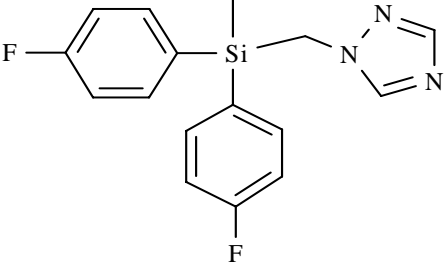
9. Updating of this review report

The technical information in this report may require to be updated from time to time in order to take account of technical and scientific developments as well as of the results of the examination of any information referred to the Commission in the framework of Articles 7, 10 or 11 of Directive 91/414/EEC. Such adaptations will be examined and finalised in the Standing Committee on Plant Health, in connection with any amendment of the inclusion conditions for flusilazole in Annex I of the Directive.

APPENDIX I

Identity, physical and chemical properties

FLUSILAZOLE

Common name (ISO)	Flusilazole
Development Code (for new actives only)	Not required
Chemical name (IUPAC)	Bis(4-fluorophenyl)(methyl)(1H-1,2,4-triazol-1-ylmethyl) silane
Chemical name (CA)	1-[[bis(4-fluorophenyl)(methyl)silyl]methyl]-1H-1,2,4-triazole
CIPAC No	435
CAS No	85509-19-9
EEC No	Not known
FAO SPECIFICATION	925 g/kg minimum and not more than ± 25 g/kg from the stated specification (AGP:CP/357)
Minimum purity	925 g/kg
Molecular formula	$C_{16}H_{15}F_2N_2Si$
Molecular mass	315.4
Structural formula	

Melting point	53.2 ± 0.06 °C *
Boiling point	Not relevant
Appearance	White crystalline solid
Relative density	1.312 ± 0.002 g/cm ³ *
Vapour pressure	3.87 · 10 ⁻⁵ Pa at 25 °C
Henry's law constant	2.7 · 10 ⁻⁴ Pa·m ³ ·mol ⁻¹
Solubility in water	41.9 mg/l at 20 °C
Solubility in organic solvents	At 25 °C: - n-hexane: > 85 g/l - acetone, ethanol, dichloromethane, methanol, ethyl acetate, xylene, acetonitrile: > 200 g/l
Partition co-efficient (log P_{ow})	pH 5: log K _{o/w} = 3.81 pH 7: log K _{o/w} = 3.87 pH 9: log K _{o/w} = 3.81
Hydrolytic stability (DT₅₀)	Stable for 34 d at pH 5, 7 and 9
Dissociation constant	pK _a : 2.5 ± 0.09
Quantum yield of direct photo-transformation in water at ε >290 nm	No absorbance in the visible spectrum, therefore not relevant
Flammability	Non flammable
Explosive properties	Not explosive
UV/VIS absorption (max.)	λ _{max} : 206 nm for neutral solutions λ _{max} : 202 nm for acidic/basic solutions
Photostability in water (DT₅₀)	Insignificant degradation at pH 7 over a 30 d period in natural sunlight. In simulated sunlight a DT ₅₀ = 60 - 80 d was calculated

APPENDIX II

END POINTS AND RELATED INFORMATION

FLUSILAZOLE

1 Toxicology and metabolism

Absorption, distribution, excretion and metabolism in mammals

Rate and extent of absorption:	Rapid and extensive (72 - 80.6 %)
Distribution:	Widely
Potential for accumulation:	Low
Rate and extent of excretion:	Rapidly excreted
Toxicologically significant compounds:	Parent compound
Metabolism in animals:	Extensively metabolised (\approx 90 %)

Acute toxicity

Rat LD ₅₀ oral:	LD ₅₀ = 674 mg/kg bw
Rat LD ₅₀ dermal:	LD ₅₀ > 2000 mg/kg bw
Rat LC ₅₀ inhalation:	LC ₅₀ = 2.7 - 3.7 mg/l in 4 h
Skin irritation:	Slight: No classification.
Eye irritation:	Reversible irritation: No classification
Skin sensitisation (test method used and result):	Non-sensitising

Short term toxicity

Target / critical effect:	Blood system, liver and urinary bladder
Lowest relevant oral NOAEL / NOEL:	0.2 mg/kg bw/d, 1 y dog
Lowest relevant dermal NOAEL / NOEL:	5 mg/kg/day, 21-day rabbit.
Lowest relevant inhalation NOAEL / NOEL:	No data presented.

Genotoxicity

Negative

Long term toxicity and carcinogenicity

Target / critical effect:	Liver and bladder
Lowest relevant NOAEL:	2 - 2.6 mg/kg bw/d, 2 y rat (long-term toxicity).
Carcinogenicity:	Testicular tumours and bladder transitional cell tumours (rat), hepatocellular tumours (mouse). NOEL for neoplasia: 125 ppm (5.03 mg/kg/day) in male rats and 375 ppm (20.05 mg/kg/day) in female rats.

Reproductive toxicity

Target / critical effect	Increased gestation length and dystocia with associated reduced pup viability and survival. Fertility parameters not affected.
Lowest relevant NOAEL / NOEL:	50 ppm (2.8 – 4.6 mg/kg/day)
Target / critical effect - Developmental toxicity:	Vaginal discharge; increased placental weight; increase in rudimentary 7 th cervical ribs.
Lowest relevant developmental NOAEL / NOEL:	0.5 mg/kg/day (rat oral developmental toxicity study).

Delayed neurotoxicity

Not required.

Other toxicological studies

Mechanistic data relating to rat bladder and testicular tumours.
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Medical data

No occupational or accidental poisoning reported.

Summary

	Value	Study	Safety factor
ADI:	0.002 mg/kg bw	1 y dog	100
AOEL systemic:	0.005 mg/kg bw/d	Oral develop. tox. rat	100
AOEL inhalation:	Not required.		
AOEL dermal (external):	0.01 mg/kg bw/d	Dermal develop. tox. rat	200
ArfD (acute reference dose):	0.005 mg/kg bw (Relevant to women of child bearing age)	Oral develop. tox. rat	100

Dermal absorption

Estimated human dermal in vivo absorption: 1% for the concentrate and 7% for the dilute product.
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2 Fate and behaviour in the environment

2.1 Fate and behaviour in soil

Route of degradation

Aerobic:

Mineralization after 100 days:

Non-extractable residues after 100 days:

Major metabolites above 10 % of applied active substance: name and/or code % of applied rate (range and maximum)

Phenyl- μ -¹⁴C + Triazole-3-¹⁴C labels-2 soil types - treatment equivalent 150 g as/ha

0.3 –0.8 % after 100 d

0.4 - 1.1 % after 1 y

16 - 22 % after 100 d

24 - 34 % after 1 y

Single metabolite:

Bis[4-fluorophenyl]methyl silanol

IN-F 7321

2.4 - 2.9 % after 100 d

max 5 % after 1 y

Supplemental studies

Anaerobic:

Phenyl- μ -¹⁴C + Triazole-3-¹⁴C label - 2 soil types - 1 mg/kg
No mineralization over 1 y

Non-extractable residues 17 - 34 % after 1 y (Silt/loam soil)
40 - 49 % after 1 year (Sandy soil)

Metabolites: 2 - 3 %

Parent material

30 - 50 % after 1 y DT₅₀ = circa 8 months (Silt /loam soil)

63 - 73 % after 1 y DT₅₀ = circa 31 months (Sandy soil)

Soil photolysis:

Phenyl- μ -¹⁴C + Triazole-3-¹⁴C label - 2 soil types - artificial + natural irradiation - Treatment equivalent to 448 g as/ha

No significant photolysis

DT₅₀ = 87 - 107 d - Average = 97 d

No significant photoproduct (max –7.6 % AR)

Remarks:

Flusilazole degradation was essentially biphasic - initially faster (circa 30 % in 100 d) followed by slow decline (10 - 15 % in 250 d)

- may be due to reduced availability to soil micro-organisms over time or decline in soil biomass levels (no determination presented). Degradation essentially results in intact flusilazole and intermediates or "bound residues". On strong extraction bound residues were shown to contain IN-F7321 fractions with considerable ¹⁴C activity with soil matrix.

Rate of degradation

Laboratory studies

DT₅₀lab (20 °C, aerobic):DT₉₀lab (20 °C, aerobic):DT₅₀lab (10 °C, aerobic):DT₅₀lab (20 °C, anaerobic):

Incubation period 1 year
circa 14 months (427 d) at 25 °C
No determination presented
No determination presented
8 - 31 months (244 - 945 d) at 25 °C Most applied AR was adsorbed to sediment (75 - 92 % of day zero samples). High soil affinity was advanced to account for high half-life values. Difference in half lives of both systems not explained, but considered to be due to microbial biomass

Field studies (country or region)

DT_{50f} from soil dissipation studies:

(1) DT₅₀ = 71 - 140 d (average 90 d) (n = 4) - bare ground
(2) DT₅₀ = 63 - 240 d (average 98 d) (n = 6) – standing crop

DT_{90f} from soil dissipation studies:

(1) > 168 - > 218 d - German soils (4) - 45 g as/ha – bare ground
(2) > 365 - > 730 d - German soils (6) - 300 g as/ha - standing crop

Soil accumulation studies:

France - continuous cropping 6 y - 1 site

g as/ha	applic/y	Final residues (mg/kg)(0-15cm)
2600 - 3000	6	0.05 - 0.09
2500	5+0	0.03 - 0.05
125/500	1	< 0.01 - 0.03

The above figures reflect the level of residue found in soils on which barley, oilseed rape and sugarbeet were grown. Samples were taken at 74, 91 and 48 days after the last application respectively for the 6-year and 1-year cycles. Samples from the 5-year treated and 1-year untreated were taken 420, 436 and 508 days after the last application respectively.

Denmark - continuous cropping 3 y - 1 site

g as/ha	applic/y	Final residues (mg/kg)(0-15cm)
1) 1500	3	0.11
2) 1500	3+0	< 0.02
3) 1200	3	0.05

The above figures reflect the level of residue found in soils on which barley and oilseed rape were grown. In 1), (3 years barley) samples were taken at 49 days after the last application. In 2), (3 years barley and 1 year no crop) samples were taken at 450 days after the last application. In 3) (2 years barley and 1 year oilseed rape) samples were taken at 49 days after the last application.

Soil residue studies:

LOQ = 0.002 mg/kg
 4 German soils - 45 g as/ha - bareground
 Day 0 0.012 - 0.065 mg/kg
 Day 100 0.002 - 0.009 mg/kg
 Day 200+ 0.002 - 0.005 mg/kg
 No significant soil residue below 0 – 20 cm

LOQ = 0.02 mg/kg
 6 German soils - 300 g as/ha - standing crop
 Day 0 0.11 - 0.21 mg/kg
 Day 100 0.05 - 0.13 mg/kg
 Day 365 0.02 - 0.07 mg/kg
 Day 730 0.02 - 0.06 mg/kg
 No significant soil residue below 0 - 10 cm

Remarks

e.g. effect of soil pH on
degradation rate

The studies presented show no apparent effect of pH on degradation rate. It is considered that soil temperature and biological activity will affect degradation rate and soil type may affect availability

Adsorption/desorption

K_f/K_{oc} :

Soil type	pH	OM%	K_{oc}	Average
Sandy loam(2)	6.5/6.6	1.1/2.1	2031 - 984	1660
Silt loam(2)	5.4/5.2	2.49/4.35	1888 - 1747	

K_d :

Sandy loam(2)	6.5/6.1	1.1/2.1	12 - 13
Silt loam(2)	5.4/5.2	2.49/4.35	47 - 76

Soil metabolites:

			<u>IN-F7321</u>	<u>IN-H9933</u>
Loamy sand	6.9	0.8	822	22
Sandy loam	6.5	2.1	605	21
Silty clay	7.6	6.9	538	15
Silt	6.3	7.5	164	8

pH dependence:

No significant pH dependence

Mobility**Laboratory studies:**

Column leaching:

Standard soils - application 60-300 g as/ha Flusilazole not detected in leachate < 0.002 mg/kg, < 0.5 µg/l (< 2 % applied)

Aged residue leaching:

Field soils (4) - application 250 g as/ha > 93 % applied ¹⁴ C retained 0.5 cm soil profile of 3 soils < 0.2 % applied ¹⁴ C in leachate In loamy sand soil (79 % sand) circa 67 % (0 - 10 cm) 88 % (0 - 15 cm) 98 % (0 - 20 cm) applied ¹⁴ C retained In one aged soil, 92 % applied ¹⁴ C retained in 0 - 5 cm and < 0.4 % recovered in leachate.
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Field studies

Lysimeter/Field leaching studies:

No study required in view of adsorption/column leaching findings.

Remarks:

Based on adsorption/column leaching studies flusilazole and its main soil metabolite IN-F7321 will be immobile in soil, with the residue mainly confined to the 0 - 10 cm soil horizon. In soil of high sand content and low organic matter residues may migrate to 0 - 20 cm profile.
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2.2 Fate and behaviour in water**Abiotic degradation**

Hydrolytic degradation:

Stable for 34 d at pH 5, 7 and 9 (25°C) (< 5 % decomposition recorded)

Major metabolites:

No data. Not required

Photolytic degradation:

Insignificant photodegradation at pH 7, over 30 d exposure to natural sunlight. In simulated sunlight at pH 7 after 30 d exposure, flusilazole accounted for 74 - 78 % AR, calculated DT ₅₀ = 60 - 80 d. No significant (circa 5 % AR) photoproducts.

Major metabolites:

No data. Not required

Biological degradation

Ready biodegradable:

Not readily biodegradable.

Water/sediment study:

DT₅₀ water:DT₅₀ (water) <<1 d (40 % in water phase at day 0)DT₉₀ water:DT₅₀ whole system:DT₅₀ (whole system): Not determined (>> 100 d)DT₉₀ whole system:Distribution in water / sediment systems
(active substance)

No detected residues in water phase

Distribution in water / sediment systems
(metabolites)

3.0 - 3.5 % AR as IN-F7321 at day 100

Relevant metabolites

Parent compound max. 96 - 98 % AR at day 14

78 - 86 % AR at day 100

Accumulation in water and/or sediment:

Parent compound persistent in sediment.

Degradation in the saturated zone

No study required.

Remarks:

Neither hydrolysis or photolysis will be a significant degradation route at environmentally relevant pH values. In aqueous systems the loss from the aqueous phase is through a binding to sediment particles.

2.3 Fate and behaviour in air**Volatility**

Vapour pressure:

 $3.866 \pm 1.7 \cdot 10^{-5} \text{ Pa at } 25 \text{ }^\circ\text{C}$

Henry's law constant:

 $2.7 \cdot 10^{-4} \text{ Pa}\cdot\text{m}^3\cdot\text{mol}^{-1}$ **Photolytic degradation**

Direct photolysis in air:

No data. Not required.

Photochemical oxidative degradation in air

DT₅₀:

20.8 hours (Atkinson calculation)

Remarks:

Due to low vapour pressure and Henry's Law Constant distribution to air is not considered significant in field use.

3 Ecotoxicology

Terrestrial Vertebrates

Acute toxicity to mammals:
Acute toxicity to birds:
Dietary toxicity to birds:
Reproductive toxicity to birds:
Short term oral toxicity to mammals:
Long term oral toxicity to mammals:

LD ₅₀ = 450 mg/kg bw - Rabbit
LD ₅₀ > 1590 mg/kg bw - Mallard Duck
LC ₅₀ = 1584 ppm - Mallard Duck
NOEC = 25 ppm - Bobwhite Quail
LD ₅₀ > 300 mg/kg bw - Rat
NOEC = 10 mg/kg bw - Rat

Aquatic Organisms

Acute toxicity fish:
Long term toxicity fish:

Bioaccumulation fish:
Acute toxicity invertebrate:
Chronic toxicity invertebrate:
Acute toxicity algae:
Chronic toxicity sediment dwelling organism:

LC ₅₀ = 1.2 mg/l - Rainbow trout
NOEClt 23 µg as/L - Fathead minnow (FFLC [252 day exp])
BCF = 205 - (peak value whole fish)
EC ₅₀ = 3.4 mg/l - Daphnia magna
NOEC = 0.27 mg/l - Daphnia magna
EC ₅₀ = 6.4 mg/l - S. capricornutum
NOEC ≥ 9.96 µg/l - Chironomus reparius

Honeybees

Acute oral toxicity:

Acute contact toxicity:

LD ₅₀ = 33.75 µg as/bee (based on Punch CS formulation)
LD ₅₀ = 165 µg as/bee

Other arthropod species

Test species
Syrphus corollae (larvae)
Coccinella septempunctatum (larvae)
Typhlodromus pyri (pre-imaginal)
Typhlodromus pyri (adult-field)
Chrysoperla carnea (larvae)
Aphidius rhopalosiphi (adult lab)

	% Effect
<i>Syrphus corollae</i> (larvae)	Harmless (38 g as/ha), minus 2% reduction in beneficial capacity
<i>Coccinella septempunctatum</i> (larvae)	Harmless (125 g as/ha), minus 60% reduction in beneficial capacity
<i>Typhlodromus pyri</i> (pre-imaginal)	Harmful (38 g as/ha), 100% mortality
<i>Typhlodromus pyri</i> (adult-field)	Harmless (180-280 g as/ha), 23-33% mortality
<i>Chrysoperla carnea</i> (larvae)	Harmless (600 g as/ha), 3% mortality
<i>Aphidius rhopalosiphi</i> (adult lab)	Harmful (600 g as/ha), 100% mortality

Earthworms

Acute toxicity:
Reproductive toxicity:

LC ₅₀ = 388 mg/kg soil
NOEC = 8.82 mg/kg soil

Soil micro-organisms

Nitrogen mineralization:

No significant adverse effect at dose levels up to 2.76 mg/kg (2000 g as/ha) over 28 d exposure

Carbon mineralization:

No significant adverse effect at dose levels up to 2.76 mg/kg (2000 g as/ha) over 31 d exposure

Litter Bag decomposition

NOEClt 107 µg as/kg soil [300 day exp]
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[Equates to plateau soil concentration following 3x200 g as /ha in cereals for 10 years]
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Appendix III**FLUSILAZOLE**

List of studies for which the main data submitter has claimed data protection and which during the re-evaluation process were considered as essential for the evaluation with a view to Annex I inclusion⁶.

B.1 Identity, B.2 Physical and chemical properties, B.3 Data on application and further information, B.4 Proposals for classification and labelling, B.5 Methods of analysis

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorisation s
2.1.6.1	Reynolds, O	1999	Determination of the water solubility (shake flask method) of flusilazole DuPont-2666 GLP: Yes Published: No	
2.1.8.0	Reynolds, O	1999	Determination of Octanol/water partition coefficient (shake flask method) of flusilazole DuPont-2663 GLP: Yes Published: No	
2.1.10.0 2.1.11.0 2.1.12.0 2.1.13.0	Gravell, R. L.	1999	Auto-flammability, flammability, explosive and oxidising properties of DPX-H6573 AMR 3338-95 GLP: Yes Published: No	
2.1.1.1	Reynolds, O.	1999	Determination of the melting point/melting range and decomposition temperature of flusilazole DuPont – 2664 GLP: Yes Published: No	
2.1.2	Reynolds, O.	1999	Determination of the density of flusilazole DuPont –2665 GLP: Yes Published: No	

⁶ List based on a detailed analysis from Ireland.

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorisations
2.1.14	Hammond, R. W.	1999	Surface tension of flusilazole DuPont –2297 GLP: Yes Published: No	
2.10	Schmucker, M.	2001	Photochemical Oxidative Degradation of Flusilazole DuPont-8703 GLP Yes Published No	

B.6 Toxicology and metabolism

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorisations
5.1.2.1	Thornley, K.T.	1998	(14C)-Flusilazole: <i>In vivo</i> dermal penetration in the rat HLO-1998-00946 GLP: Yes Published: No	
5.1.2.2	John, S.A.	1998	(14C)-Flusilazole: Rates of penetration through human and rat skin using an <i>in vitro</i> system HLO-1998-00945 GLP: Yes Published: No	
5.2.5.1	Finlay, C.	1998	Flusilazole Technical (DPX-H6573): Primary Eye Irritation Study in Rabbits DuPont report HL-1998-01720 GLP: Yes Published: No	
5.6.2.2	Cook J.C., Hurtt, M.E., Munley, M.A.	1998	Dermal developmental Toxicity Study of Flusilazole in Rats: A Summary of the Compound-Related Effects and a Discussion of the Possible Mechanism of Action DuPont report dated March 27 1998 GLP: Yes Published: No	

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorisations
5.6.2.3	Schardein, J.L.	1998	A Dermal Prenatal Developmental Toxicity Study of Flusilazole in Rats HLO 1998-01504 (2 volumes) GLP: Yes Published: No	
5.6.2.4	Munley, S.M.,	2000	Flusilazole Technical: Developmental Toxicity Study in rats. DuPont-2287; GLP: Yes Published: No	
5.3.1.1	Elwell, M.R.	1998	One-Year Feeding Study in Dogs with INH-6573. Supplement No. 1. DuPont report HLR-461-85, Supplement No.1 GLP: Yes Published: No	

B.7 Residue data

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorisations
6.1.5	Smyser, B.P., Moghaddam, M.F.	1997	Metabolism of Phenyl and triazole flusilazole in sugar beet. AMR 2994-94 GLP: Yes Published: No	

B.7 Fate & Behaviour

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorisations
7.1.4	Singles and Russell	1998	Long-Term Terrestrial Field Dissipation of (Phenyl(U)14C)DPX-H6537 at Stine Farm, Delaware AMR 556-86, Supplement No. 1 GLP: No Published: No	

B.9 Ecotoxicology

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not	Reports on previous use in granting national authorisations
8.2.2	Hoke, R.	2000	Flusilazole Technical: Early Life-Stage Toxicity to Rainbow Trout, <i>Oncorhynchus mykiss</i> Dupont-3319 GLP: Yes Published: No	
8.2.2	Rhodes, J. E.	2003	Flusilazole (DPX-H6573) Technical: Full Life-Cycle Toxicity Test with the Fathead Minnow, <i>Pimephales promelas</i> , Under Flow-Through Test Conditions Dupont-5577 GLP Yes	
8.2.2	Ellis, R.J.	2003	Flusilazole (DPX-H6573) Technical: Study to Evaluate the Effects on the Synthesis of Vitellogenin (VTG) and on the Development of Gonads in male and Female Fathead Minnows (<i>Pimephales promelas</i>) Dupont-11370 GLP in part	
8.2.2	Dinter, A.	2003	Flusilazole: Risk Assessment For Fish Under Chronic Exposure Conditions Dupont-12096	
8.2.2	Foerster, B	2002	Carbendazim/flusilazole (DPX-N7872) SE (1:2) Effects on the decomposition of organic matter in the field DuPont-5820 GLP Yes	

8.2.7	Forster, A.	1999	¹⁴ C-Flusilazole: to assess the toxicity to the sediment dwelling phase of the midge <i>Chironomus riparius</i> DuPont-1155 GLP: Yes Published: No	
8.4.2	Gossman, A	1999	Flusilazole 25g/L EW, Effects on reproduction and growth of the earthworm, <i>Eisenia fetida</i> in artificial soil Dupont-2131 GLP Yes Published No	
8.5	Foerster, B	2001	Carbendazim/flusilazole (DPX-N7872) SE (1:2) Effects on the decomposition of organic matter in the field DuPont-5820 –interim	
8.6	Kölzer, U.	2003	Flusilazole (DPX-H6573) 25EW: Effects on the Decomposition of Organic Matter in the Field Dupont-11052 GLP Yes	

APPENDIX IV**List of uses supported by available data****Flusilazole**

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/ha min max	water l/ha min max	kg as/ha min max		
Winter Wheat, and Rye	EU	'Sanction' 'Punch C'	F	Eyespot and Foliar diseases	EC SC	400g/L 250 g/L	Medium vol spray	GS 71	3	28	N/A	200	0.16	Defined by GS at latest application	
Winter Barley and Oats	EU	'Sanction' 'Punch C'	F	Eyespot and Foliar diseases	EC SC	400g/L 250 g/L	Medium vol spray	GS 59	2	28	N/A	200	0.2	Defined by GS at latest application	
Sugar Beet	EU	'Punch CS' 'Punch 40'	F	Eyespot and Foliar diseases	SE EC	400 g/L 250 g/L	Medium vol. spray	Full crop cover	2	28	N/A	200	0.15	49	
Maize	EU	'Punch C'	F	Eyespot and Foliar diseases	EC	250 g/L	Medium vol. pray	Flowe ring	2	21	N/A	200	0.2	28	
Oilseed rape	EU	'Punch C'	F	Eyespot and Foliar diseases	EC	250 g/L	Medium vol. spray	Petal fall	2	21 days	N/A	200	0.2	50	

- Remarks:**
- (a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
 - (b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
 - (c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
 - (d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
 - (e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
 - (f) All abbreviations used must be explained
 - (g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
 - (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
 - (i) g/kg or g/l
 - (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
 - (k) The minimum and maximum number of application possible under practical conditions of use must be provided
 - (l) PHI - minimum pre-harvest interval
 - (m) Remarks may include: Extent of use/economic importance/restrictions