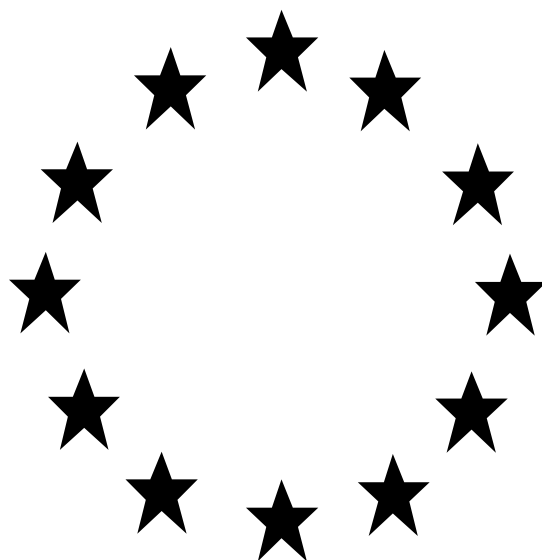




Draft Assessment Report (DAR)

- public version -

**Initial risk assessment provided by the rapporteur Member State
The Netherlands for the existing active substance**

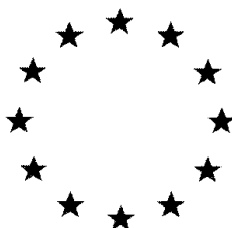
PYRIDABEN

**of the third stage (part B) of the review programme
referred to in Article 8(2) of Council Directive 91/414/EEC**

Volume 1

August 2007

European Commission



PYRIDABEN

VOLUME 1

Rapporteur Member State: The Netherlands

March 2007

Draft Assessment Report and Proposed Decision of the Netherlands prepared in the context of the possible inclusion of pyridaben in Annex I of Council Directive 91/414/EEC

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INTRODUCTION

Pyridaben is an insecticide and acaricide which is effective against mites and whiteflies in orchard citrus and greenhouse tomatoes.

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LEVEL 1

Pyridaben

STATEMENT OF THE SUBJECT MATTER AND PURPOSE OF THE MONOGRAPH

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1 Statement of subject matter and purpose for which the monograph was prepared**1.1 Purpose for which the monograph was prepared (dossier Document A)**

This monograph on the active substance pyridaben has been prepared to support the inclusion of the active substance pyridaben in Annex I of the Directive 91/414/EEC.

1.2 Summary and assessment of information relating to the collective provision of dossiers (Dossier Document B)

Nissan Chemical Industries, Ltd. is the sole notifier for pyridaben. The question of steps taken to collectively present the dossier does not therefore arise.

1.3 Identity of the active substance (Annex IIA 1) (Dossier Documents J, K-II and L-II)**1.3.1 Name and address of applicant(s) for inclusion of the active in Annex I (Annex IIA 1.1)****Applicant (name, address, etc.)**

Address: Nissan Chemical Europe S.A.R.L.
Parc d'affaires de Grécy
2, rue Claude Chappe
69370 St-Didier-au Mont-d'Or
France

Contact person:

Tel.no.: [REDACTED]

Fax no.: [REDACTED]

Email: --

1.3.2 Common name and synonyms (Annex IIA 1.3)

Common name: Pyridaben (ISO)

Synonyms: NC-129, BAS 300 I, BAS 9078 I

1.3.3 Chemical name (Annex IIA 1.4)

IUPAC: 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one

CA: 4-chloro-2-(1,1-dimethylethyl)-5-[[[4-(1,1-dimethylethyl)phenyl]methyl]thio]-3(2H)-pyridazinone

1.3.4 Manufacturer's development code number (Annex IIA 1.5)

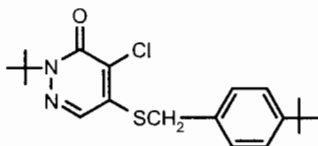
NC-129, BAS 300 I, BAS 9078 I

1.3.5 CAS, EEC and CIPAC numbers (Annex IIA.1.6)

CAS no.: 96489-71-3

EEC no.: 405-700-3

CIPAC no.: 583

1.3.6 Molecular and structural formulae, molecular mass (Annex IIA 1.7)**Molecular formula:** C₁₉H₂₅ClN₂OS**Molecular mass:** 364.9**Structural formula:****1.3.7 Manufacturer or manufacturers of the active substance (Annex IIA 1.2)**

Name Factory:

Address:

Contact person:

Email: - -

Location of plant

See Volume 4, Annex C (Confidential Information).

1.3.8 Method or methods of manufacture (Annex IIA 1.8)

See Volume 4, Annex C (Confidential Information).

1.3.9 Specification of purity of the active substance (Annex IIA 1.9)

The minimum content of pure active substance pyridaben in the manufactured material under industrial scale production and used for production of formulated products is 980 g/kg $\approx$ 98 wt %.

1.3.10 Identity of isomers, impurities and additives (Annex IIA 1.10)

See Volume 4, Annex C (Confidential Information). There are no relevant impurities identified.

1.3.11 Analytical profile of batches (Annex IIA 1.11)

See Volume 4, Annex C (Confidential Information).

1.4 Identity of the plant protection products (Annex IIA 3.1; IIIA 1) (Dossier Documents J, K-II, L-II, K-III and L-III)**1.4.1 Current, former and proposed trade names and development code numbers (Annex IIIA 1.3)**

Trade names: Nexter Pro, Sanmite 75 WP

Code names: Pyridaben 75WP in WSB, NC-129 75 WP in WSB, BAS 300 19 I

1.4.2 Manufacturer or manufacturers of the plant protection product (Annex IIIA 1.2)

Name Factory:

Address:

Contact person:

Email: - -

Location of plant

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

Contact person:

[REDACTED]
[REDACTED]

Fax no.: - -

Email: - -

1.4.3 Type of the preparation and code (Annex IIIA 1.5)

WP: Wettable Powder

GIFAP code: WP

1.4.4. Function (Annex IIA 3.1; Annex IIIA 1.6)

Insecticide, Acaricide

1.4.5 Composition of the preparation (Annex III 1.4)

See Volume 4, Annex C (Confidential Information).

**1.5 Use of the plant protection product (Annex IIA 3.2 to 3.4; Annex IIIA 3.1 to 3.7, 3.9 and 12.1)
(Dossier Documents C, D and E)**

1.5.1 Field of use (Annex IIA 3.3; Annex IIIA 3.1)

Field (citrus) and glasshouse (tomato)

1.5.2 Effects on harmful organisms (Annex IIA 3.2; Annex IIIA 3.2)

Pyridaben is orally and/or percutaneously taken into mobile forms of insects (whiteflies, mites). Pyridaben rapidly paralyzes and kills the pests within 24 hours when treated at concentrations for practical uses. In addition, pyridaben quickly stops the embryonic development of whiteflies/mites and kills embryos when treated on eggs.

1.5.3 Summary of intended uses (Annex IIA 3.4; Annex IIIA 3.3 to 3.7, 3.9)

See Table 1.5.3-01.

1.5.4 Information on authorization in EU Member States (Annex IIIA 12.1)

Pyridaben as an insecticide and acaricide is authorised in Belgium, Czech Republic, France, Greece, Hungary, Italy, The Netherlands, Poland, Portugal, Slovakia and Spain.

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Table 1.5.3-01 Summary of intended uses (Annex IIA 3.4; Annex IIIA 3.3 - 3.7, 3.9)

Summary of representative uses evaluated (pyridaben)

Crop and / or situation (a)	Member State or Country	Product name	F or 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		
Citrus	Southern MS	Nexter Pro, Sanmite 75 WP	F	Mites Whitefly	WP	750 g/l	Tractor mounted / trailed broadcast air assisted sprayer	At infestation on No later than BBCH 83	1	na	0.005 – 0.04	750 - 6000	0.3	14
Tomato	Northern and Southern MS	Nexter Pro, Sanmite 75 WP	G	Mites Whitefly	WP	750 g/l	Various hydraulic sprayers	At infestation on No later than BBCH 89	1	na	0.005 – 0.04	625 - 5000	0.25	3

- (a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
- (b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
- (c) e.g. biting and sucking 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 plant- type of equipment used must be indicated

- (i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**
- (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) Indicate the minimum and maximum number of application possible under practical conditions of use
- (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha)
- (m) PHI - minimum pre-harvest interval

LEVEL 2

Pyridaben

OVERALL CONCLUSIONS

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2 Reasoned statement of the overall conclusions drawn by the Rapporteur Member State

2.1.1 Identity

All points of Section 1, Annex IIA and IIIA have been addressed.

2.1.2 Physical and chemical properties

Pyridaben pure is a white crystalline solid at room temperature with a melting temperature of 109.4 to 110.6°C. Thermal decomposition starts at 200°C and the vapour pressure was determined to be $<1 \times 10^{-5}$ Pa at 25°C. Pyridaben Technical is a white crystalline powder. The (technical) substance is not flammable nor autoflammable and has no oxidizing properties. Pyridaben is sensitive to friction and is considered to present a danger of explosion (However a new study on explosive properties is in progress). The log Pow at 23°C is >6.37 . Pyridaben is hydrolytically stable under typical environmental conditions (pH 5.0, 7.0 and 9.0) and does not dissociate. Its quantum yield is 0.0304 and the DT50 for photolysis in water during irradiation with Xenon light is 6.8 minutes.

Pyridaben 75WP in WSB (750 g/kg Pyridaben) is a tan, light beige/grey fine powder. The product is not flammable not autoflammable and has neither explosive properties nor oxidizing properties. The pH of a 1% dispersion is 8.7 to 8.8. An accelerated storage test of 14 days at 54°C, 8 weeks at 40°C and 98 days at 50°C, a shelf-life study of 1 year at 25°C and 2 years at ambient conditions have determined the physico-chemical stability of the product.

2.1.3 Details of uses

Pyridaben is an insecticide and acaricide to be used in agriculture for the control of insects and mites on citrus orchards and greenhouse tomatoes and is orally and/or percutaneously taken into mobile forms of insects (whiteflies, aphids, mites) when treated via contact or residual. Pyridaben is basically regarded as a non-systemic product.

Details of further information

Information supplied addresses methods for handling and storage of the active substance and plant protection product.

2.1.4 Classification and labelling

Pyridaben is sensitive to friction and is considered to present a danger of explosion (E, R2). However a new study on explosive properties is in progress.

Based on the provided toxicological information, the RMS proposes the following risk/safety phrases and hazard symbols for classification and labelling of pyridaben relating to human health effects.

Hazard symbol	:	T
Indications of danger	:	Toxic
Risk phrases	:	R23; Toxic by inhalation. R25; Toxic if swallowed.
Safety phrases	:	S22; Do not breathe dust. S37; Wear suitable gloves. S38; In case of insufficient ventilation, wear suitable respiratory equipment. S45; In case of accident or if you feel unwell seek medical advice immediately (show the label where possible)

Justification for the proposal

R23	Based on the results of the acute inhalation toxicity study.
R25	Based on the results of the acute oral toxicity studies.
S22	Recommended for substances which are supplied in the form of an inhalable dust.
S37	Obligatory for toxic substances.
S38	Obligatory for substances labelled with R23.
S45	Obligatory for substances labelled with R23 or R25.

Based on the provided toxicological information, the RMS proposes the following risk/safety phrases and hazard symbols for classification and labelling of Nexter Pro relating to human health effects.

Hazard symbol	:	Xi, T ⁺
Indications of danger	:	Irritant; Very toxic
Risk phrases	:	R22; Harmful if swallowed. R26; Very toxic by inhalation. R41; Risk of serious damage to eyes.

Safety phrases	:	S22; Do not breathe dust. S26; In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S36; Wear suitable protective clothing. S37; Wear suitable gloves. S38; In case of sufficient ventilation, wear suitable respiratory equipment. S39; Wear eye/face protection. S45; In case of accident or if you feel unwell seek medical advice immediately (show the label where possible).
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Justification for the proposal:

R22	Based on the results of the acute oral toxicity study.
R26	Based on the results of the acute inhalation toxicity study.
R41	Based on the results of the eye irritation study.
S22	Recommended for formulations which are supplied in the form of an inhalable dust.
S26	Obligatory for substances labelled with R41.
S36	Obligatory for very toxic formulations.
S37	Obligatory for very toxic formulations.
S38	Obligatory for very toxic formulations.
S39	Obligatory for substances labelled with R41.
S45	Obligatory for very toxic formulations.

Based on the provided ecotoxicological information, the RMS proposes the following risk/safety phrases and hazard symbols for classification and labelling of pyridaben relating to ecotoxicological effects.

In acute toxicity tests with technical pyridaben in fish, *Daphnia magna* and algae, the lowest LC/EC50 values were 0.73, 1.0 and >13 µg/L, respectively. Pyridaben has a log Pow value of >3, but the experimentally determined BCF is <100 (B.9.2.3). Pyridaben was however not ready biodegradable (B.8.4.3). It is proposed, that on the basis of its acute toxicity pyridaben should be categorised as "Dangerous for the environment" (N), "Very toxic to aquatic organisms" (R50) and "May cause long-term adverse effects in the aquatic environment" (R53).

It is recommended that the active substance also carries the following 'S' safety phrases:

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 sheet

In acute toxicity tests with the Pyridaben 75 WP formulation in fish, *Daphnia magna* and algae, the lowest LC/EC50 values were 2.9, 1.3 and 46000 µg product/L, respectively. Pyridaben has a log Pow value of >3.0, but the experimentally determined BCF is <100 (B.9.2.3). Pyridaben was however not ready biodegradable (B.8.4.3). It is proposed, that on the basis of its acute toxicity the Pyridaben 75 WP formulation should be categorised as "Dangerous for the environment" (N), "Very toxic to aquatic organisms" (R50) and "May cause long-term adverse effects in the aquatic environment" (R53).

It is recommended that the Pyridaben 75 WP formulation also carries the following 'S' safety phrases:

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 sheet

2.2 Methods of analysis

2.2.1 Analytical methods for analysis of the active substance as manufactured

A HPLC-UV method was submitted for the determination of pyridaben in technical material. This method was comparable to CIPAC method 583 for the determination of pyridaben in technical material and in wettable powders. The validation results fulfilled the criteria.

2.2.2 Analytical methods for formulation analysis

A HPLC-UV method was submitted for the determination of pyridaben in the plant protection product. This method was comparable to CIPAC method 583 for the determination of pyridaben in technical material and in wettable powders. The validation results fulfilled the criteria.

2.2.3 Analytical methods for residue analysis

Treated plants, plant products, foodstuffs, feeding stuffs

The data for GC-ECD method D9309 support an LOQ (pre- and post-registration) of 0.05 mg/kg for orange fruit and orange process products (orange peel, orange oil, orange molasses, wet and dried orange pulp, orange juice, marmalade, canned orange). The data for GC-ECD method D9312 support an LOQ (pre-registration) of 0.05 mg/kg for tomato, where the LC-MSMS method for oranges can be used for confirmation.

No acceptable methods for products of animal origin were submitted. Since no residues are expected in animal products, further questions are redundant.

Residues in body fluids and tissues

As pyridaben is classified as toxic, methods validated in blood and tissues are required. The method for the determination of pyridaben, PB-7 and PB-9 in animal products, which used a methylation step with diazomethane, is acceptable for pyridaben when the methylation step is excluded, except that a confirmatory method has not been provided.

Soil, water and air

Fully validated methods for determination of pyridaben in soil (LC-MS/MS, LOQ 0.01 mg/kg), water (LC-MS/MS, LOQ of 0.005 µg/L) and air (HPLC-UV, LOQ 1 µg/m³) were submitted. These methods are suitable for pre- and post-registration monitoring. The LOQ of 0.005 µg/L for surface water is below the level of the lowest appropriate toxicity value for aquatic organisms (in this case the NOEC for daphnia (0.086 µg/L). The method in air is considered suitable for post-registration monitoring because the LOQ (1 µg/m³) is below the limit of 1.2 µg/m³ calculated using: limit = $AOEL_{systemic} \cdot 0.1 \cdot 60 / 10$ (based on a daily respiratory volume of a worker of 10 m³ and an $AOEL_{systemic}$ of 0.002 mg/kg bw/day).

Additional methodology for the metabolites included in the residue definitions for water, soil and air should be submitted unless non-inclusion of the metabolites in these residue definitions is decided (potential data gap).

2.3 Impact on human and animal health

2.3.1 Effects having relevance to human and animal health arising from exposure to the active substance or impurities contained in the active substance or to their transformation products

This toxicological dossier contains studies with the test substance pyridaben, which is also known under the name NC-129, Sanmite or Nexter.

2.3.1.1 Toxicokinetics

In all studies available [3,6-pyridazinone-ring-¹⁴C]-pyridaben and [benzyl ring-¹⁴C]-pyridaben were studied in parallel. In case no differences between the findings for both compounds were present the text gives a single range and/or refers to ¹⁴C-pyridaben.

Absorption

In three studies with Sprague Dawley rats 168 hours after a single oral dose of 3 and 30 mg/kg bw, or 14-day repeated oral dosing at 3 mg/kg bw, 80-97% AR was excreted with faeces. In urine concentrations of applied radioactivity were 3-4% after [3,6-pyridazinone-ring¹⁴C]-pyridaben and 11-19% after low dose [benzyl ring¹⁴C]-pyridaben and slightly higher after 30 mg/kg bw [benzyl ring¹⁴C]-pyridaben (13-24%). In expired air very low amounts of radioactivity were recovered (<0.07% AR). In tissues 5-11% AR was retained after 2 hours and <1.4% AR 168 hours after a single dose ¹⁴C-pyridaben. Peak ¹⁴C-concentrations in blood were observed after 12 hours in both sexes after an oral single or repeated dose of 3 mg/kg bw, but only after 24 hours after a single oral dose of 30 mg/kg bw. Oral absorption was found to be 3-5% and 11-19% after low dose [3,6-pyridazinone-ring¹⁴C]-pyridaben and [benzyl ring¹⁴C]-pyridaben, respectively, and 3-7% and 13-24% after high dose [3,6-pyridazinone-ring¹⁴C]-pyridaben and [benzyl ring¹⁴C]-pyridaben, respectively. Actual absorption might have been higher because of the fact that excretion via the entero-hepatic circulation was not taken into account (no bile-duct cannulation and analysis of radioactivity in bile). No differences between the sexes were observed.

In another study with Sprague Dawley rats 67-84% AR was retained from faeces 72 hours after a single dose of 30 mg/kg bw ¹⁴C-pyridaben, whilst radioactivity in urine accounted for 4-6% AR after dosing [3,6-pyridazinone-ring¹⁴C]-pyridaben and 14-24% after dosing [benzyl ring¹⁴C]-pyridaben. Oral absorption based on recovered radioactivity in urine, liver, skin and carcass is estimated to be 5-7% and 15-27% for [3,6-pyridazinone-ring¹⁴C]-pyridaben and [benzyl ring¹⁴C]-pyridaben, respectively. Bile-duct cannulation was not included in the study design. After cannulation of the bile-duct of additional groups of rats in the same study (single dose 30 mg/kg bw), radioactivity in bile accounted for 22-30% AR. In faeces (and the gastro-intestinal tract) and in urine 56-72% AR and 1.6-4.0% AR, respectively, were recovered. A statistical significance difference between males and females for urine and bile (benzyl ring label) ($p < 0.01-0.05$) and between both radiolabels for urine and faeces ($p < 0.01$) was found. Based on the results of this study it can be concluded that absorption via the gastro-intestinal tract is 26-39% AR, based on %AR in bile, urine, skin and carcass.

A much higher absorption (49-57%) was found in another study with Wistar rats receiving a single dose of 3 mg/kg bw. In this study the bile-duct of the rats was cannulated. After 48 hours biliary and faecal excretion accounted for 47-56% and 45-51% of the applied radioactivity, respectively. Urinary excretion was 1-5.7% AR.

From the studies with bile-duct cannulation it can be concluded that oral absorption after a single low dose is 49-57% and 26-39% after a single high dose. However, it is not clear whether the difference in absorption rate was caused by the height of the dose or by the use of two different

strains of rats with a strain dependent different absorption. In these studies no consistent differences between the sexes or both radiolabels were reported.

As the liver is not the main target organ, the %AR in bile should not be included in the final oral absorption rate. Therefore, based on %AR in urine, skin and carcass, oral absorption amounts to 11-19%. Although a direct effect on liver was not seen in the repeated dose toxicity studies with pyridaben, the working mechanism of pyridaben is very aspecific (inhibition of mitochondrial electron transport) and an effect on liver cannot completely be ruled out. Data on elimination through bile were available. Based on %AR in bile, urine, skin and carcass oral absorption amounts to 26-39% for 30 mg/kg bw, and 49-57% for 3 mg/kg bw, the latter being measured over 48 hours, whereas the other studies had a duration of 168 hours. The majority of %AR passed the bile within the first 6 hours.

Considering the fact that the working mechanism is aspecific, it is considered too worst-case to take the lowest level for oral absorption. However, it is also concluded that the amount excreted in bile should not be included in the total oral absorption, as the liver is not the critical effect. Relevant absorption for risk assessment purposes will be between 10 and 30%. Therefore, the highest amount of oral absorption of the low dose based on urine, skin and carcass will be considered for risk assessment purposes, being 20%.

Elimination

In three studies with Sprague Dawley rats 168 hours after a single oral dose of 3 and 30 mg/kg bw, or repeated oral dosing at 3 mg/kg bw, the majority of administered radioactivity was excreted in faeces (80-97% AR), whilst radioactivity in urine accounted for 3-19% AR and in expired air for <0.07% AR. Pre-treatment for 14 days did not affect the pattern of excretion and retention.

In another study 72 hours after a single dose of 30 mg/kg bw ¹⁴C-pyridaben 67-84% AR was retained from faeces and 4-6% AR from urine after dosing [3,6-pyridazinone-ring¹⁴C]-pyridaben and 14-24% from urine after dosing [benzyl ring¹⁴C]-pyridaben.

The elimination half-life of [3,6-pyridazinone-ring¹⁴C]-pyridaben was longer than that for [benzyl ring¹⁴C]-pyridaben: 23 hours versus 9-10 hours after a single dose of 3 mg/kg bw, 60-70 hours versus 12 hours after repeated dosing and 49-56 hours versus 18-24 hours after a single dose of 30 mg/kg bw. No differences between the sexes became apparent.

Distribution

In one study, at 2 hours after a single oral dose of 3 mg/kg bw, low radioactivity concentrations were found in tissues (4-10% and 5-6% AR after [3,6-pyridazinone-ring¹⁴C]-pyridaben and [benzyl ring¹⁴C]-pyridaben, respectively). The highest amounts were recovered from liver (563 and 1150 ng eq./g (1.0-2.1 % AR), 1250-1330 ng eq./g (2.0-2.9% AR) after [3,6-pyridazinone-ring¹⁴C]-

pyridaben and [benzyl ring¹⁴C]-pyridaben, respectively). In other organs radioactivity ranged from 256-392 ng eq./g (kidneys), 1110 and 2170 ng eq./g (uterus), 896-3290 ng eq./g (ovary) and 849-1390 ng eq./g (lymph nodes). Concentrations decreased rapidly thereafter.

In a second study 24 hours after a single dose of 30 mg/kg bw a comparable pattern of distribution to that after a single oral dose of 3 mg/kg bw was shown. The concentrations in high dose rats were on average a factor of 12 and 17 for [3,6-pyridazinone-ring¹⁴C]-pyridaben and [benzyl ring¹⁴C]-pyridaben, respectively, higher than in low dose rats (hence roughly proportional to the dose). In a separate study with 30 mg/kg bw (single dose) radioactivity recovered from liver and kidney was 6 and 11 times higher than that recovered after a single dose of 3 mg/kg bw, again reasonably proportional to dose.

After repeated oral administration of 3 mg/kg bw radioactivity in tissues 168 after the last dose was below 0.1% AR.

There were no remarkable differences between tissue levels and depletion rates of male and female rats.

Metabolism

Three studies are available using TLC analysis and co-elution of reference compounds as analytical method. The analyses were stated to be confirmed by two-dimensional TLC, but the results were not adequately included in the reports. The fourth study uses either HPLC or TLC to separate the metabolites and confirmed metabolites by co-elution of reference compounds or LC-MS.

All metabolites identified were <5% AR except for the parent in faeces, P-9 and B-11 in urine and two unknowns.

In 0-48 hour urine of rats treated with [3,6-pyridazinone-ring¹⁴C]-pyridaben (single oral dose or repeated dosing of 3 mg/kg bw), which contained 2-3% AR, no metabolites were identified and confirmed. Metabolites identified by TLC included parent, P-9, P-1, P-3 and PB-12. After a single dose of 30 mg/kg bw [3,6-pyridazinone-ring¹⁴C]-pyridaben P-9 was identified and confirmed by LC-MS in 0-72 hour urine (total 2-6% AR). In addition parent, P-1, P-3, P-7, PB-3, PB-9, PB-11 and PB-12 were identified by TLC or HPLC. The metabolite pattern was essentially the same for both sexes.

In urine of rats treated with a single dose of 3 or 30 mg/kg bw [benzyl ring¹⁴C]-pyridaben or treated repeatedly with 3 mg/kg bw (0-48 hour after low dose (6-14% AR) and 0-72 hour after high dose (12-24% AR)) B-11 was identified and confirmed by LC-MS. Several other metabolites were present and identified by TLC or HPLC including B-1 and B-8 and in addition parent, B-3, B-7, B-15, PB-4, PB-7, PB-8, PB-12. The metabolite pattern was essentially the same for both sexes and dosing regimes.

In faeces of rats treated with [3,6-pyridazinone-ring¹⁴C]-pyridaben (total radioactivity 45-54% AR low dose, 61-91% AR high dose) the parent and PB-12 were identified. At 30 mg/kg bw the parent (confirmed by LC-MS) was the main component accounting for >10% AR. In addition PB-3, PB-4, PB-7, PB-8, PB-9, PB-11, P-1 and P-3 were identified by TLC or HPLC, but not further confirmed. No major differences between sexes or dosing regimes could be found.

After treatment with [benzyl ring¹⁴C]-pyridaben TLC or HPLC analysis showed the parent to be the main component of faeces (13-32%). In addition B-1, B-3, B-7, B-8, B-11, B-15, PB-3, PB-4, PB-7, PB-9, PB-11, PB-12 and D-1 were found, but not confirmed adequately. Total radioactivity in faeces was 57-68% AR after a single dose and 35-42% AR after repeated dosing.

In liver the parent was recovered after HPLC analysis after a single dose at 30 mg/kg bw [3,6-pyridazinone-ring¹⁴C]-pyridaben (total radioactivity 0.7% AR). TLC analysis did not show any metabolites. After [benzyl ring¹⁴C]-pyridaben (single dose of 3 or 30 mg/kg bw) B-1 was identified after TLC and HPLC analysis. In addition parent, B-3, B-7, B-8, B-11, PB-4, PB-9, PB-12 and PB-13 were found. In bile PB-8 was found after a single dose of 30 mg/kg bw [3,6-pyridazinone-ring¹⁴C]-pyridaben. No metabolites were found after [benzyl ring¹⁴C]-pyridaben.

In three studies, metabolites were poorly separated on the TLC plates and not accurately confirmed. This renders the studies supplementary. However, all studies combined do provide information on the metabolic pattern of pyridaben. In the fourth study (at 30 mg/kg bw ¹⁴C-pyridaben) metabolites separated by HPLC could not be sufficiently identified by co-chromatography of referent compounds. In this study accurate confirmation of identity by LC-MS was available for P-9 and B-11 in urine and the parent compound in faeces.

Dermal absorption data

The dermal absorption of Pyridaben in rats *in vivo* was 8.9% and 2.7% after a single dermal application of respectively 7.5 µg/cm² (actual 2.3 µg/cm²) and 5 mg/cm² (actual 4.77 mg/cm²). Comparison of rat and human skin data indicate that dermal absorption through rat skin is about 7.2 fold greater than through human skin, for the low dose level (spray dilution). For the high dose level (concentration at mixing and loading), no data were available.

Considering the results from the *in vivo* and *in vitro* dermal absorption studies, for occupational risk assessment purposes, a dermal absorption of 1.2% should be considered for test substance concentration of approximately 1.5-7.5 µg/cm² (e.g. spray dilution of BAS 300 11 I (i.e. Nexter Pro)) and 0.4% for test substance concentrations of approximately 5 mg/cm² (e.g. concentrated formulation during mixing and loading).

2.3.1.2 Toxicodynamics

Acute toxicity

Pyridaben needs to be classified as toxic if swallowed (T, R25) on the basis of its acute oral toxicity in rats and as toxic after inhalation (T, R23) on the basis of its acute inhalatory toxicity in rats. Pyridaben does not need to be classified on the basis of its acute dermal toxicity and is considered not irritating to the skin and eyes, and not a skin sensitiser (Maximisation and Buehler tests).

Short-term and semi-chronic toxicity

Three weeks of dermal exposure of rats to 0, 30, 100, 300 and 1000 mg/kg bw/day resulted in decreased body weight gain at 300 and 1000 mg/kg bw/day. The NOAEL for systemic effects was set at 100 mg/kg bw/day.

After subacute inhalation exposure of rats to 0, 1, 3 and 10 mg/m³, reduced body weight was observed at 10 mg/m³. Based on these effects a NOAEL of 3.0 mg/m³ was established for systemic effects.

Dietary exposure of rats to 0, 30, 65, 155 and 350 mg/kg food/day of pyridaben (equal to 0, 2.3, 4.9, 11.6 and 25.7 mg/kg bw/d for males and 0, 2.6, 5.5, 12.8 and 27.7 mg/kg bw/day for females) for 13 weeks caused decreased body weight gain at 65 mg/kg food in females and at 155 and 350 mg/kg food in both sexes. Food and water consumption were decreased at 155 and 350 mg/kg food. Food conversion efficiency was also decreased at 155 and 350 mg/kg food in both sexes and at 65 mg/kg food in females. No toxicological significant changes were noted in haematology. At clinical biochemistry, gamma glutamyltransferase was increased at 350 mg/kg food in both sexes. Alkaline phosphatase was increased at 350 mg/kg food in females at the end of the exposure period and in males at the end of the recovery period. Total protein was decreased at 65 mg/kg food in females and at 155 and 350 mg/kg food in both sexes. Albumin was decreased in females at 65, 155 and 350 mg/kg food. Albumin/globulin ratio was slightly increased in males at 350 mg/kg food. α 1-Globulin concentration was increased and α 2- and β -globulin concentrations were decreased in males at 350 mg/kg food. The NOAEL is established at 30 mg/kg food (equal to 2.7 mg/kg bw/d for females) based on decreased body weight gain and changes at clinical biochemistry (decreased protein and albumin).

Dietary exposure of mice to 0, 30, 90, 270 and 810 mg/kg food (equal to 0, 4.1, 13.0, 40.1 and 119.2 mg/kg bw/d for males and 0, 4.9, 14.6, 43.1 and 124.6 mg/kg bw/d for females) for 13 weeks, caused reduced body weight gain and water consumption at 90 mg/kg food and above. Food consumption and food conversion efficiency were decreased from 180 and 90 mg/kg food

onwards, respectively. Changes in haematology (a.o. decreased haematocrit and haemoglobin) were noted at 810 mg/kg food. Changes in clinical biochemistry were noted at 270 mg/kg food and above and included changes in ALP, ASAT, OCT, urea, total protein, chloride and phosphorus. Changes in relative organ weights were noted at 270 and 810 mg/kg food, but were considered to be due to the decreased body weight gain. Histopathology revealed acute inflammation and necrosis of the liver in all groups including control. A NOAEL of 30 mg/kg food is established (equal to 4.1 mg/kg bw/day in males and 4.9 mg/kg bw/day in females) based on decreased body weight gain.

Dogs exposed to 0, 0.5, 1.0, 4.0 and 16.0 mg/kg bw/d of pyridaben in a gelatin capsule for 3 months showed a dose-related increased incidence of food-like emesis and ptyalism at 4.0 and 16.0 mg/kg bw/d. Body weight gain was reduced at 4.0 and 16.0 mg/kg bw/d in males. Food consumption was reduced in all treated males but this was not dose-related. Mild lymphoid hyperplasia was noted in 2/4 males at 16.0 mg/kg bw/d. The NOAEL is set at 1.0 mg/kg bw/d based on decreased body weight gain, food-like emesis and ptyalism.

Dogs exposed to 0, 0.5, 1.0, 4.0, 16.0 and 32.0 mg/kg bw/d of pyridaben in a gelatin capsule for 12 months showed a reduced body weight gain at 1.0-32.0 mg/kg bw/d in both sexes and at 0.5 mg/kg bw/d in females. A high variation in body weight and body weight gain was observed within groups and between groups, also between the two control groups. The variation in food consumption was also high. An increased incidence of soft stool was noted at 4.0 mg/kg bw/d and above. Food-like emesis and ptyalism were observed at all dose levels, including control group, with an increased incidence and higher severity at higher dose levels.

In view of the large variation in body weights at the start of the experiment, the decrease in body weight gain at 0.5 and 1.0 mg/kg bw/d is considered to be no adverse effect. The NOAEL is set at 1.0 mg/kg bw/d based on decreased body weight gain.

In conclusion, in all rodent and dog studies with oral, dermal and inhalation exposure decreased body weight (gain) was the adverse effect.

Considering the identity of the observed effects at the LOAELs after oral, dermal and inhalation repeated exposure, classification with R48 is not considered necessary.

Genotoxicity

Pyridaben did not induce point mutations in *S. typhimurium* tester strains TA98, TA100, TA1535 and TA1537 and in the *Escherichia coli* tester strain WP₂uvrA, both with and without metabolic

activation. Pyridaben was negative in an *in vitro* chromosome aberration test with a Chinese hamster ovary cell line CHO. Pyridaben was negative in a gene mutation test using Chinese hamster cells. In addition, pyridaben was negative in an *in vitro* DNA repair study using male rat hepatocytes, pyridaben was also negative in an *in vivo* mouse micronucleus test. In conclusion, pyridaben is considered non-genotoxic.

Long-term toxicity

In a 2-year combined toxicity/carcinogenicity study in rats, administration of pyridaben at 0, 4, 10, 28 and 80 (oncogenicity group)/120 (toxicity group) mg/kg food (equal to 0, 0.2, 0.4, 1.1 and 3.2-5.0 mg/kg bw/day in males and 0, 0.2, 0.5, 1.5 and 4.2-6.5 mg/kg bw/day in females) resulted in reduced body weight and food consumption at 80 and 120 mg/kg food. Leukocyte count was decreased at 10-120 mg/kg food in females. Neutrophils were decreased at 4 mg/kg food in females and at 10-120 mg/kg food in both sexes. Observed changes in leucocytes and neutrophils were considered to be due to bacterial infection and not test substance related. Urine volume was decreased and specific gravity was increased in males at 120 mg/kg food. Protein content was increased at 120 mg/kg food in females and increased in both sexes in the course of the study. Absolute testes weight was increased at 120 mg/kg food in the toxicity group and ovary weight was increased at 80 mg/kg food in the oncogenicity group.

Based on reduced body weight, food consumption and food conversion, the NOAEL is set at 28 mg/kg food (equal to 1.1 mg/kg bw/day in males and 1.5 mg/kg bw/day in females). No oncogenic potential of the test substance in rats was observed.

In a 78-week carcinogenicity study in mice, pyridaben was administered via the diet at 0, 2.5, 8.0, 25 or 80 mg/kg food (equal to 0, 0.27, 0.81, 2.78 and 8.88 mg/kg bw/day for males and 0, 0.29, 0.91, 2.78 and 9.74 mg/kg bw/day for females). Treatment at 80 mg/kg food resulted in slightly reduced survival in males. Body weight gain was decreased at 80 mg/kg food in both sexes and at 25 mg/kg food in males. Food conversion efficiency during the first 14 days of the study was lower at 80 mg/kg food in both sexes.

No oncogenic potential was observed in mice. Based on reduced body weight gain a NOAEL of 8.0 mg/kg food (equal to 0.81 and 0.91 mg/kg bw/d for males and females, resp.) is established.

Reproduction and developmental toxicity

In an oral 2-generation reproduction study in rats (0, 10, 28 and 80 mg/kg food), a decrease in body weight gains and food consumption was noted among males and females from the F₀- and F₁-generation at 80 mg/kg food. An increase in absolute ovary weight was observed at 28 and 80 mg/kg food and accompanied by an increase in relative ovary weight at 80 mg/kg food in the F₀-

generation. There were no changes observed between parental animals of the treated and control groups in mating indices, pregnancy rates, fertility, oestrus cycle, post-implantation loss and macroscopic findings.

Examination of the F_0 and F_1 -offspring revealed decreased body weights of pups at 80 mg/kg food in weeks 3 and 4 post partum. No treatment-related changes were detected in clinical signs, litter size, birth weight, sex ratio, litter survival, pup development, auditory and visual responses or macroscopic observations of the F_0 and F_1 -offspring. Based on the data presented in this study, the NOAEL for parental toxicity was 28 mg/kg food (equivalent to 1.87 mg/kg bw/day). The NOAEL for developmental toxicity was 28 mg/kg food (equivalent to 5 mg/kg bw/day). The NOAEL for reproductive toxicity was considered to exceed 80 mg/kg food (equivalent to 5.33 mg/kg bw/day).

In a teratogenicity study in rats (0, 2.5, 5.7, 13.0 and 30.0 mg/kg bw/day) the NOAEL for maternal effects was 5.7 mg/kg bw/day (equal to 4.7 mg/kg bw/day after correction for measured concentration of the test substance), based on decreased body weight gain and food consumption. The NOAEL for developmental effects was set at 13.0 mg/kg bw/day (equal to 12.5 mg/kg bw/day after correction for measured concentration of the test substance), based on decreased mean foetal weight, and retarded ossification of various bones. No treatment-related effects were observed on the number of corpora lutea or implantations, the number of live foetuses, and the sex ratio. There were no morphological changes observed in foetuses that could be attributed to treatment. Therefore, the NOAEL for teratogenicity was considered to exceed 30.0 mg/kg bw/day (equal to 26.7 mg/kg bw/day after correction for measured concentration of the test substance).

In an oral teratogenicity study in rabbits (0, 1.5, 5 and 15 mg/kg bw/day), a NOAEL for maternal effects of 5 mg/kg bw/day was derived, based on body weight loss and decrease in body weight gain, slightly reduced food consumption and reduced faeces. Since no effects on foetal development and no irreversible structural effects were noted, the NOAEL for developmental and teratogenic effects was set at 15 mg/kg bw/day.

In a dermal teratogenicity study in rabbits (0, 70, 170 and 450 mg/kg bw/day), the NOAEL for local maternal effects was <70 mg/kg bw/day, based on moderate to severe erythema and/or slight eschar formation at 70 mg/kg bw/day. The NOAEL for systemic maternal effects was set at 70 mg/kg bw/day, based on decreased body weight and food consumption. Since no effects on foetal development and no irreversible structural effects were noted, the NOAEL for developmental and teratogenic effects was set at 450 mg/kg bw/day.

Neurotoxicity

In an acute neurotoxicity study in rats (0, 50, 100 and 200 mg/kg bw by gavage), no mortality was observed. Animals given 100 and 200 mg/kg bw showed piloerection, hypoactivity, tremors and partially closed eyes, mainly on the day of administration. No clinical signs were observed from day 4 onwards. Body weight gains were reduced in males and females given 100 and 200 mg/kg bw. Food consumption was reduced on the day of dosing in all treated males and females. In the functional observation battery a lower activity, weak startle reflex, weak flexor responses were noted at day 1 in males at 100 and 200 mg/kg bw. Furthermore, an increased incidence of slow or poorly coordinated righting reflex was noted in males at 200 mg/kg bw and reduced body temperature in females at 100 mg/kg bw and both sexes at 200 mg/kg bw. No changes in landing foot splay, grip strength and motor activity were observed. Macroscopic post mortem examination and histopathological examination of the central and peripheral nervous system did not reveal any abnormalities.

Based on the clinical observations and changes in FOB at 100 and 200 mg/kg bw, the NOAEL for acute toxicity is set at 50 mg/kg bw. Observed changes are likely to result from overt toxicity, rather than from specific neurotoxicity.

Dietary exposure of rats to 0, 30, 100 or 350 mg/kg food (equal to 0, 2.5, 8.5 and 28.8 mg/kg bw/day in males, and 0, 2.8, 9.3 and 31.1 mg/kg bw/day in females) for 13 weeks, caused reduced body weight gains in males and females given 350 mg/kg food. Food consumption was reduced in males and females given 350 mg/kg food. No treatment-related findings were noted in the functional observation battery, grip strength and motor activity tests. Macroscopic post mortem examination and histopathological examination of the central and peripheral nervous system did not reveal any abnormalities.

Based on the changes in body weight at 350 mg/kg food, the NOAEL is set at 100 mg/kg food (equal to 8.5 mg/kg bw/day in males and 9.3 mg/kg bw/day in females). No signs of neurotoxicity were observed, hence to the NOAEL for neurotoxicity is 350 mg/kg food (28.8 mg/kg bw/d).

Mechanistic data

To further evaluate the effect of pyridaben on several body functions additional tests were conducted.

The first study was conducted to clarify why salivation was seen in the dog studies performed. From this 13-week study, in which 300 mg/kg bw was administered by stomach-soluble or small intestine-soluble capsule. Pyridaben causes decreased food consumption and body weight loss when given in a stomach-soluble capsule, but not in a small intestine-soluble capsule. In none of the animals salivation was observed. However, the effects observed regarding salivation do not

coincide with the 90-day and 1-year dog studies (paragraph 6.3.4). Moreover, mortality was high at 300 mg/kg bw in an earlier 13-week study (Project no. IRDC 563-005, 1989), while no mortality was observed at this level in the current study. Therefore, no conclusion can be drawn on salivation.

In the other two studies a number of body functions were studied in several animal species after administration of a single dose intragastrically, ocular or intradermal, or in *in vitro* experiments.

Pyridaben induced behavioural changes in rats at 100 mg/kg bw and higher, and in mice at 30 mg/kg bw and higher. Pyridaben resulted in reduced brain activity, reduced body temperature, in rats at 300 mg/kg bw, increased sleeping time at 100 mg/kg bw in mice. A decreased respiration rate and heart rate and decreased blood pressure compared to the control group was found at 30 and 300 mg/kg bw in rats. No change in blood pressure, blood flow, electrocardiogram and heart rate were observed in dogs at doses up to 300 mg/kg bw. Pyridaben did not influence contraction of the gastrocnemius muscle after electric stimulation of the sciatic nerve in rats at doses up to 300 mg/kg bw. Pyridaben did reduce food consumption after 24 hours at 30 and 300 mg/kg bw in rats, but not after 6 hours. Pyridaben reduced traction force at 300 mg/kg bw in rats; coordinative motion was not influenced. No reduction in corneal reflex was seen after ocular administration in guinea pigs, while skin twitch reflex was reduced in 1 guinea pig after intradermal application. A reduced reflex after tail pinching was seen in mice and reflex was almost nullified after intraperitoneal injection of acetic acid at 100 mg/kg bw. Pyridaben did increase the pH of gastric juice at 300 mg/kg bw, but not the volume produced in rats. Mobility through the small intestine was not influenced by pyridaben in mice. Bile volume was not influenced by pyridaben in rats. Pyridaben resulted in a reduced urine volume at 30 and 300 mg/kg bw in rats.

Pyridaben did inhibit contraction of isolated guinea pig ileum, especially histamine-induced contractions. Pyridaben did inhibit noradrenalin-induced contraction of the isolated vas deferens from guinea pigs, but not electrically stimulated contraction. Pyridaben did not influence coagulation of rabbit blood, but it did influence haemolysis. The flow rate in an isolated rabbit ear vein was not influenced by pyridaben. Chronotropic effects of isoproterenol on contractions of atria preparations from guinea pigs were negatively influenced by pyridaben. Pyridaben did reduce contractile force of the isolated rat fundus. Pyridaben induced reduced oxytocin-induced contractions of the uterus from non-pregnant rats, while spontaneous contractions of the uterus from pregnant rats were not influenced.

Toxicological data with metabolites

Metabolite PB-7 showed to be less toxic than pyridaben for acute oral toxicity. PB-7 was negative in an Ames test and in a lethal DNA damage test with bacteria.

Formulation data

According to the Directive 2001/59/EC, BAS 300 11 I needs to be classified as very toxic after inhalation (T+, R26) on the basis of its acute inhalatory toxicity in rats.

BAS 300 11 I is not irritating to the skin. Irreversible effects on the cornea in one eye irritation study, were considered to be due to mechanical effects of the powder, as this was not observed when the eyes were washed 7 hours after instillation in a similar eye irritation test. Since washing is permissible for solids, according to OECD 405, BAS 300 11 I is considered not irritating to the eye. In a Buehler test BAS 300 11 I is not a skin sensitizer.

2.3.2 ADI

The ADI has to be derived from the results of toxicity studies with experimental animals. The calculation of the ADI is based on the highest dose at which no adverse effect is observed in the most appropriate study in the most sensitive species. Pyridaben was tested in several subacute, semi-chronic and chronic studies in dogs, rats and mice, in a reproduction study in rats, and in teratogenicity studies in rats and rabbits. Furthermore, it was established in several *in vitro* and *in vivo* genotoxicity tests that pyridaben does not have genotoxic potential.

The overall critical effect of pyridaben was considered to be reduced body weight (gain). Several repeated dose studies, including the 2-generation reproduction toxicity study and teratogenicity studies were considered for the establishment of the ADI (Table 2.3.2-01).

Table 2.3.2-01 Studies considered for the establishment of the ADI

Study	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Reference
Semichronic toxicity studies			
13-week, oral, rat (diet)	2.6 (F)	5.5 (F)	Holmes, 1988a
13-week, oral, mouse (diet)	4.1 (M)	13.0 (M)	Holmes, 1988b
3-month, oral, dog (capsule)	1.0	4.0	Spicer, 1989b
1-year, oral, dog (capsule)	1.0	4.0	Spicer, 1990, 1991 incl additional study
Chronic toxicity studies			
2-year, oral, rat	1.1 (M)	5.0 (M)	Holmes, 1990a
78-week, oral, mouse	0.81 (M)	2.78 (M+F)	Holmes, 1990b
Reproduction and teratogenicity studies			
2-generation, oral, rat	Parental: 1.87 Developmental: 5	5.33 15	Willoughby, 1990
Teratogenicity, oral, rat	Maternal: 4.7	12.5	Willoughby, 1990
Teratogenicity, oral, rabbit	Maternal: 5	15	Ross, 1988

In all semichronic, chronic and reproduction and teratogenicity studies the critical effect is reduced body weight (gain). The NOAELs for all studies – independent of exposure duration – are comparable (about 1 mg/kg bw/d), differences only appear because of the choice of dose levels. Therefore, the relevant NOAEL for derivation of the ADI is 1 mg/kg bw/d. A safety factor of 100 for inter- and intraspecies differences is applied, resulting in an ADI of 0.01 mg/kg bw/day.

Note: Since similar effects were observed in rats, mice, rabbits and dogs, one could consider applying only a safety factor of 10 for intraspecies differences. However, in the absence of relevant human data (see also Guidance for the setting of AOELs, 5 July 2005, European Commission), a safety factor of 100 for inter- and intraspecies differences is applied.

2.3.3 ARfD (acute reference dose)

According to the Guidance for the setting of an Acute Reference Dose (Document 7199/VI/99 rev. 5) an ARfD should not be allocated if:

- the pesticide has shown a very low acute oral toxicity (e.g. no adverse clinical signs and deaths have been observed at the limit dose for acute LD₅₀ testing), and
- the toxicological profile was based only on e.g. mild effects, which are not relevant for acute intake (e.g. adaptive liver enlargement, chronic body weight reduction, reduced food intake), and
- the toxicological profile has no other alerts for acute toxicity.

Furthermore, residue data should be taken into account to conclude on the necessity of an ARfD.

Based on the submitted data on pyridaben, the following considerations were made:

- The lowest acute oral LD₅₀ of pyridaben was found to be 161 mg/kg bw in male rats and 181 mg/kg bw in females rats.
- In the acute neurotoxicity study, overt signs of toxicity were noted at doses of 100 mg/kg bw/day, including clinical signs, reduced body weight, lower activity, weak startle reflex and flexor responses.
- In mechanistic studies, a.o. effects on activity, respiration rate, blood pressure, heart rate, were observed after single doses of 30 mg/kg bw in rats and mice.

Based on the above data, it can be concluded that the criteria for not allocating an ARfD are not met, since the LD₅₀ value is <2000 mg/kg bw and alerts for acute toxicity were observed. From the acute LD₅₀ studies in mice, the acute neurotoxicity study in rats and the acute mechanistic studies in mice (and rats showed similar effects) it is clear that acute exposure to pyridaben results in

acute effects, including body weight changes, changes in activity and reflexes, changes in respiration rate, heart rate and blood pressure. Therefore, the allocation of an ARfD is considered justified.

The calculation of the acute reference dose is based on the highest dose at which no adverse effect is observed in the most appropriate acute toxicological endpoint of relevance to humans, derived from the most appropriate study in the most appropriate species.

The following studies were considered relevant for the establishment of the ARfD:

- The acute oral LD₅₀ studies in mice in which a NOAEL of 31 mg/kg bw could be established. Signs of toxicity observed in both sexes at 50 mg/kg bw (LOAEL) were mortality, decreased locomotor movement, prone and/or crouching posture and ataxia.
- The acute neurotoxicity study in rats: a NOAEL of 50 mg/kg bw/day was established. At 100 (LOAEL) and 200 mg/kg bw clinical signs (piloerection, hypoactivity, tremors and closed eyes), reduced body weight, no locomotion and weak reflexes were noted.
- Acute mechanistic studies in mice with a NOAEL of 10 mg/kg bw. Females at 30 mg/kg bw (LOAEL) showed diarrhoea, abnormal body posture, decreased response to touch, decreased motor activity, abnormal gait, decreased muscle tone and abnormal respiration within 1 hour after administration and the effects disappeared within 24 hours. Males showed similar clinical signs and loss of startle reflex at 100 mg/kg.
- Acute body function study in rats with a NOAEL of 3 mg/kg. At 30 mg/kg a decreased respiration rate, heart rate and blood pressure was seen. A similar experiment in dogs showed no effect on heart rate, electrocardiogram, blood flow and blood pressure up to 300 mg/kg bw.
- The teratogenicity study in rats: a NOAEL of 4.7 mg/kg bw/d was established for maternal effects and 12.5 mg/kg bw/d for developmental effects. Only a non-specific effect of decreased body weight gain and food consumption in dams were noted at the LOAEL of 12.5 mg/kg bw/d. Decreased foetal weight and retarded ossification of various bones was observed at 26.7 mg/kg bw/d.
- The teratogenicity study in rabbits: a NOAEL of 5 mg/kg bw/day was established for maternal effects and 15 mg/kg bw/d for developmental effects. Only a non-specific effect of decreased body weight gain in dams was noted at the LOAEL of 15 mg/kg bw/d and no effects were observed in offspring.

The most relevant NOAEL for the derivation of the ARfD is considered the NOAEL of 5 mg/kg bw/day, based on a comparison of NOAELs and LOAELs of the studies described above. Application of a safety factor of 100 for inter- and intraspecies differences results in an ARfD of 0.05 mg/kg bw/day.

2.3.4 AOEL

Nexter Pro is used on citrus in the field and on tomato in glasshouses as a spray.

Application of Nexter Pro on citrus and tomato takes place once during or before growth stage BBCH 83 and 89, respectively. As multiple cultures might be produced within one year in glasshouses, chronic use of Nexter Pro cannot be excluded.

Exposure of bystanders can be excluded for use on tomatoes, since Nexter Pro is used in glasshouses. Exposure of bystanders cannot be excluded for use on citrus fruit.

For the use of Nexter Pro, re-entry activities should be considered for citrus and tomato. For tomato crops in glasshouses, it cannot be excluded that exposure will be several times per year.

Pyridaben was tested in several semi-chronic and chronic oral studies in dogs, rats, and mice, in a reproduction study in rats and in teratogenicity studies in rats and rabbits (see Table 2.3.4-01).

Table 2.3.4-01 Studies considered for the establishment of the AOEL

Study	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Reference
Dermal and inhalation toxicity studies			
28-day, inhalation, rat	0.84 ¹ (3.0 mg/m ³)	2.7 ¹ (10 mg/m ³)	Hoffman, 1989
28-day, dermal, rat	100	300	Blaszczak, 1992
Semichronic toxicity studies			
13-week, oral, rat (diet)	2.6 (F)	5.5 (F)	Holmes, 1988a
13-week, oral mouse (diet)	4.1 (M)	13.0 (M)	Holmes, 1988b
3-month, oral, dog (capsule)	1.0	4.0	Spicer, 1989b
1-year, oral, dog (capsule)	1.0	4.0	Spicer, 1990, 1991 incl additional study
Chronic toxicity studies			
2-year, oral, rat	1.1 (M)	5.0 (M)	Holmes, 1990a
78-week, oral, mouse	0.81 (M)	2.78 (M+F)	Holmes, 1990b
Reproduction and teratogenicity studies			
2-generation, oral, rat	Parental: 1.87 Developmental: 5	5.33 15	Willoughby, 1990
Teratogenicity, oral, rat	Maternal: 4.7	12.5	Willoughby, 1988
Teratogenicity, oral, rabbit	Maternal: 5	15	Ross, 1988
Teratogenicity, dermal, rabbit	Maternal: 70	170	Hellwig, 1995

¹ based on an respiratory volume of 9 L/h and body weight of 200 g (TNO-report V98/390 d.d. December 1998, Default values in occupational risk assessment)

As pyridaben is extensively metabolised, route-specific toxicity cannot be excluded. Therefore, if available, toxicity studies for the route concerned should be considered to calculate route-specific AOELs. In case of pyridaben subacute dermal and inhalation studies were available.

In a 28-day inhalation study, a NOAEL of 3.0 mg/m³ (equivalent to 0.84 mg/kg bw/day) was established for systemic effects. The observed effects at the LOAEL of 10 mg/m³ (2.7 mg/kg bw/day) were equivalent to the effects observed after oral exposure, mainly body weight effects. The effect levels for both oral and respiratory route are in the same order of magnitude. Therefore, it is concluded that derivation of a specific AOEL for respiratory exposure is not considered necessary.

In a 21-day dermal toxicity study, a NOAEL of 100 mg/kg bw/day was derived, based on decreased body weight gain. As the application area was 25 cm², the area concentration is 4 mg/cm² at the NOAEL, hence a dermal absorption of 2.7% is applicable. Based on this dermal absorption an internal dose of 2.7 mg/kg bw/day can be calculated for the dermal study, which is higher than the internal dose for the oral route. Therefore, as a worst-case, the oral NOAEL is used for the establishment of the AOEL.

The working mechanism of pyridaben is very aspecific, namely inhibition of mitochondrial electron transport. Considering the effect levels in subacute, semichronic and chronic oral toxicity studies in rats, dogs and mice, there seems to be no effect of exposure duration after oral administration of pyridaben. Therefore, all repeated dose studies can be considered as starting point for the derivation of the AOEL. The overall NOAEL for pyridaben is considered to be approximately 1 mg/kg bw/day for both semichronic and chronic exposure of operators, bystander and/or workers.

Application of a safety factor of 100 for intra- and interspecies differences, results in an external AOEL of 0.01 mg/kg bw/day. As oral absorption is assumed to be 20% (see B.6.1.4), correction is made for oral absorption, resulting in a systemic AOEL of 0.002 mg/kg bw/day (0.12 mg/day for a 60 kg person, and 0.14 mg/day for a 70 kg person).

Note: Since similar effects were observed in rats, mice, rabbits and dogs, one could consider applying only a safety factor of 10 for intraspecies differences. However, in the absence of relevant human data (see also Guidance for the setting of AOELs, 5 July 2005, European Commission), a safety factor of 100 for inter- and intraspecies differences is applied.

2.3.5 Drinking water limit

According to Council Directive 97/57/EC, exposure to pyridaben through the drinking water should account for not more than 10% of the ADI. If it is assumed that the average daily consumption of water amounts to 2 litre per person of 60 kilogram, a drinking water limit of (60x0.01)/10)/2 mg/l,

i.e. 0.03 mg/l can be calculated, However, according to Document 8064/VI/79 of the European Commission, the EU drinking water limit for pesticides of 0.1 µg/l is applicable for pyridaben.

Since aquatic metabolite PB-7 is less toxic than pyridaben, no drinking water limit for PB-7 is established.

2.3.6 Impact on human or animal health arising from exposure to the active substance or to impurities contained in it

Nexter Pro is used as an insecticide in citrus and tomato, and contains 750 g pyridaben/kg product. In citrus, Nexter Pro is applied outdoors, by mechanical upward spraying (mist blower, motor pump spray gun or high pressure rotary sprayer). In tomato, Nexter Pro is applied indoors, by manual up- and downward spraying.

In exposure assessments for including an active substance on Annex I, first, exposure estimates using appropriate modelling systems should be considered. Exposure estimates can be derived using the published models, which reflect European conditions.

Operator exposure values without and with personal protective equipment (PPE) were calculated using the UK and the German model. Both the UK and the German model have no data available for indoor applications. Therefore, the Dutch Glasshouse model was used.

As no bystanders should be allowed in greenhouses during the application of Nexter Pro, therefore, no estimation of bystander exposure for manual up- and downward spraying in greenhouses will be made (tomato). For Nexter Pro, bystander exposure should be considered for application in citrus. For bystander exposure during mechanical upward spraying, no formally approved models exist. As an estimate, the draft values proposed for the EUROPOEM II, 2002 model were used.

For the use of Nexter Pro re-entry activities should be considered for harvesting and sorting of citrus and tomatoes. Exposure during re-entry activities in citrus and tomato is estimated using the EUROPOEM II model and some dislodgable foliar residue calculations.

A risk assessment for the operators, workers and bystanders has been made. The results of these preliminary risk assessments are presented in table 2.3.6-01 to -03.

Table 2.3.6-01 Operator internal exposure and risk assessment

Model	Route	Estimated internal exposure (mg a.s./day)		AOEL-systemic (mg a.s./day)	% AOEL	
		without PPE	with PPE		without PPE	with PPE
Mechanical upward spraying on citrus						
UK- 75 th	Respiratory	0.12	0.12	0.12	50	50
	Dermal	0.58	0.41	0.12	242	167
	Total exposure	0.70	0.53	0.12	292	217
DE- GM	Respiratory	0.06	0.06	0.14	45	45
	Dermal	0.35	0.03	0.14	250	22
	Total exposure	0.41	0.09	0.14	295	67
Manual up- and downward spraying on tomato (indoor)						
NL-glasshouse	Respiratory	0.03	0.003	0.14	18	2
	Dermal	0.06	0.006	0.14	43	4
	Total exposure	0.09	0.009	0.14	61	6

Table 2.3.6-02 Bystander internal exposure and risk assessment

Table 10: Estimated internal exposure and non assessment			
Route	Estimated internal exposure (mg a.s./day)	AOEL systemic (mg a.s./day)	% AOEL
Exposure during mechanical upward spraying on citrus			
Respiratory	0.015	0.14	11
Dermal	0.036	0.14	26
	0.051	0.14	36
Total exposure			
Exposure during manual up- and downward spraying on tomato			
should be prohibited			

Table 2.3.6-03 Worker internal exposure and risk assessment

Table 2.10.3.3 Worker internal exposure and risk assessment					
Route	Estimated internal exposure		AOEL	% AOEL	
	(mg a.s./day)		Systemic		
	without PPE	with PPE	(mg a.s./day)	without PPE	with PPE
Mechanical upward spraying on citrus					
Respiratory	-	-	0.14	-	-
Dermal	0.042	0.004	0.14	30	3
Total exposure	0.042	0.004	0.14	30	3
Manual up- and downward spraying on tomato (indoor)					
Respiratory	0.0825	0.0083	0.14	59	6
Dermal	0.225	0.023	0.14	161	16
Total exposure	0.308	0.031	0.14	220	22

Conclusions

- For mechanical upward spraying on citrus, it is concluded that a safe use was identified for operators with PPE for mechanical upward spraying on citrus, using the German model.
- For manual up- and downward spraying on tomato (indoor), it is concluded that a safe use was identified for operators without PPE for manual up- and downward spraying on tomato, using the Dutch Glasshouse model.
- For bystander exposure during mechanical upward spraying on citrus, it is concluded that a safe use was identified for bystanders for mechanical upward spraying on citrus, using the EUROPOEM II model (90th percentile).
- No bystanders should be allowed in greenhouses during the application of Nexter Pro on tomatoes.
- For worker exposure during re-entry activities in citrus, it is concluded that a safe use was identified for workers without PPE during re-entry activities in citrus, using the EUROPOEM II.
- For worker exposure during re-entry activities in tomato, it is concluded that a safe use was identified for workers with PPE during re-entry activities in tomato, using EUROPOEM II.

2.4 Residues

2.4.1 Definition of the residues relevant to MRLs

Plant products

The residue definition in citrus and tomato for post-registration monitoring and for risk assessment is proposed as Pyridaben.

Animal products

A goat metabolism study was performed at a 1N and 10N dose level showing that pyridaben was the major residue in tissue and milk. Since no residues are expected in animal tissue, a residue definition for animal products is not needed.

2.4.2 Residues relevant to consumer safety

Residues in products of plant origin

Complete residue data sets were present for tomato (greenhouse) and orange (field) and MRLs of 0.1 and 0.2 mg/kg were calculated, respectively

Pyridaben was shown to be stable under conditions simulating pasteurisation, baking/brewing/boiling and sterilisation. Processing factors (pyridaben residues) were <1 for washed whole oranges (max 0.66), molasses (0.30), orange juice (max 0.14), marmalade (max 0.21) and canned fruit (max <0.12). Residues were concentrated in wet pomace (max x1.11), dry pomace (max x5.16) and orange oil (x25.3). Processing studies in tomatoes are not required as residue levels are <0.1 mg eq/kg. The statement on tomato is subject to revision pending on the generation of new residue data under least favourable conditions.

Residues in products of animal origin

The concentration in animal feed is 0.17 mg/kg at the highest, which is lower than the lowest dose in the goat metabolism study and 15 times lower than the lowest dose in the cow feeding in which no residues above the LOQ were found in animal products. Based on this assessment it is expected that no residue definition for animal products will be required and no MRLs need to be set.

Residue intakes by livestock animals and humans

Intakes by livestock animals

Intake of residues by dairy cattle and beef cattle may be expected from wet pomace only (tomato is not a constituent of cattle feed). Residue intakes were calculated using a HR-P of 0.13 mg/kg. The calculated TMDI for beef cattle was 0.0073 mg/kg bw/day (0.17 mg/kg diet dry weight) based on a HR (whole fruit, oranges) of 0.12 mg/kg and a wet pomace processing factor of 1.1. Wet pomace and tomato is not a constituent of poultry and pig diet.

Intake by humans

Consumer chronic risk assessment show acceptable risks for the WHO-EU consumer diet (2.1% ADI) and the UK adult (9.1% ADI) and UK-toddler diet (35.4% ADI). Consumer acute intake show acceptable risks for all consumer groups with the UK-toddler giving the highest risk (23.8% ARfD for orange).

2.4.3 Residues relevant to worker safety

See toxicology section.

2.4.4 Proposed EU MRLs and compliance with existing MRLs

Community MRLs are proposed for orange (0.2 mg/kg) and tomato (0.1 mg/kg). Before MRLs can be calculated for mandarin and lemon, at least 4 additional trials according to cGAP with mandarin are required.

2.4.5 Proposed EU import tolerances and compliance with existing MRLs

Not applicable, since no non-EU applications are proposed in the intended use pattern.

2.4.6 Basis for differences, if any, in conclusions reached having regard to established or proposed CAC MRLs

Not applicable, since no Codex MRLs have been established or proposed yet.

WARNING: This document forms part of an EU evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

2.5 Fate and behaviour in the environment

2.5.1 Definition of the residues relevant to the environment

Detailed guidance to define the environmental residue is not available. Provisionally therefore, the active substance and major metabolites are listed in the definition. No metabolites were formed at >10% AR under aerobic laboratory conditions in soil treated with pyridaben, but PB-4 and PB-7 exceeded 5% AR at 2 consecutive time points (and are hence relevant for exposure of groundwater). The metabolite PB-22 was found at levels up to 13% AR in irradiated soil samples but not in dark controls, and is hence relevant for exposure of soil. PB-7 reached maximum levels in water and sediment of 17% AR and 14% AR respectively. Major aqueous photodegradates of pyridaben were W-1 (max. 27.9% AR, DT₅₀ <1.5 hours, therefore not included in residue definition for air) and B-3 (max. 29.2% AR, photolytically stable).

The components of the environmental residue are therefore as follows:

Soil:	pyridaben, PB-22
Surface Water:	pyridaben, PB-7, W-1, B-3
Sediment:	pyridaben, PB-7
Ground water:	pyridaben, PB-4, PB-7, PB-22
Air:	pyridaben, PB-22, PB-7, B-3

2.5.2 Fate and behaviour in soil

Aerobic degradation

In laboratory studies on aerobic incubation of pyridaben at 20°C in four soils (pH 6.0-7.6, 0.8-3.8% oc), pyridaben degraded with DT₅₀ values of 50-199 days (persistence) and 65-1104 days (non normalised - modelling). DT₉₀ (persistence) values were 241-4522 days. During aerobic incubation of pyridaben at 10°C in one soil (pH 6.0, 0.8% oc), pyridaben degraded with a DT₅₀ value of 279 days (persistence & modelling) and a DT₉₀ (persistence) value of 926 days.

No metabolite accounted for >10% AR at any time. Metabolites exceeding 5% AR at 2 consecutive time points were PB-4 (maximum 7.6% AR) and PB-7 (maximum 8.5% AR). DT₅₀ values for PB-4 and PB-7 could not be estimated.

Table 2.5.2-01 presents a summary of the available DT₅₀ (persistence) and DT₉₀ (persistence) values of pyridaben. Modelling DT₅₀ values are given in Table 2.5.2-02. This table also presents moisture corrected DT₅₀ (modelling) values.

Table 2.5.2-01 Laboratory DT₅₀ (persistence) and DT₉₀ (persistence) values for the aerobic degradation of pyridaben in soil, at 20°C

Substance	soil	pH	% oc	Moisture	dose (mg/kg)	temp. (°C)	DT ₅₀ (d)	DT ₉₀ (d)	kine-tics	DT ₅₀ (20°C, d)	DT ₉₀ (20°C, d)
Pyridaben	sandy loam ¹	6.2	2.4	40% mwhc	0.48	20	132	597	DFOP	132	597
	sandy loam ²	6.2	2.4	40% mwhc	0.50	20	181	778	DFOP	181	778
	mean									157	688
	clay loam	7.6	3.8	40% mwhc	0.51	20	50	241	DFOP	50	241
	silt loam	6.7	1.9	40% mwhc	0.51	20	199	4522	FOMC	199	4522
	sandy loam	6.0	0.8	40% mwhc	0.51	20	80	2057	DFOP	80	2057
overall mean										121	1877

FOMC = First Order Multi-Compartment model

DFOP = Double-First-Order in Parallel model

¹ Treatment with benzene-labeled 14C-pyridaben

² Treatment with pyridazinone-labeled 14C-pyridaben

Table 2.5.2-02 Laboratory DT₅₀ (modelling) values for the aerobic degradation of pyridaben in soil, at 20°C

at 20 °C										
substance	soil	pH	% oc	Moisture	dose (mg/kg)	temp. (°C)	DT ₅₀ (d)	kine-tics	DT ₅₀ (20°C, d)	DT ₅₀ (20°C, d) pF 2/10 kPa ³
Pyridaben	sandy loam ¹	6.2	2.4	40% mwhc	0.48	20	135	SFO	135	
	sandy loam ²	6.2	2.4	40% mwhc	0.50	20	181	SFO	181	
	mean								158	106.4
	clay loam	7.6	3.8	40% mwhc	0.51	20	65	SFO	65	37.6
	silt loam	6.7	1.9	40% mwhc	0.51	20	171	SFO	171	104.1
	sandy loam	6.0	0.8	40% mwhc	0.51	20	95.0	SFO	95.0	63.9
	overall geometric mean									

SFO = Single First-Order model

¹ Treatment with benzene-labeled 14C-pyridaben

² Treatment with pyridazinone-labeled 14C-pyridaben

³ Details on the methods to calculate moisture corrected DT50 (modelling) values are presented in section B.8.6.3 (PEC_{GW} estimations), in particular Table B.8.6.3-02.

Mineralisation of pyridaben (Ben-label) in one soil at 20°C represented 18% AR on day 90 (21% AR on day 150). Mineralisation of pyridaben (Pyr-label) at 20°C amounted to 10% AR on day 90 (15% AR on day 151) in one soil, but in three other soils only 0.1-3.3% AR on day 90-120 (0.2-3.4% AR on day 150-151). Non-extractable residues however at 20°C never exceeded 70% AR: for pyridaben Ben-label (one soil) and Pyr-label (4 soils) 12-31% AR after 90-120 days, 13-37% AR after 150-151 days, max. 16-37% AR.

Aerobic metabolism of pyridaben proceeds due to microbial processes involving oxidation giving PB-4, PB-7 and PB-9. The sulphide and sulfoxide bridges are hydrolysed producing metabolites with either the benzene or the pyridazinone ring. PB-14 and PB-22 are formed by rearrangement. The ultimate breakdown products are CO₂ and non-extractable residues. Figure 2.5.2-01 shows the proposed metabolic pathway with the main degradation products.

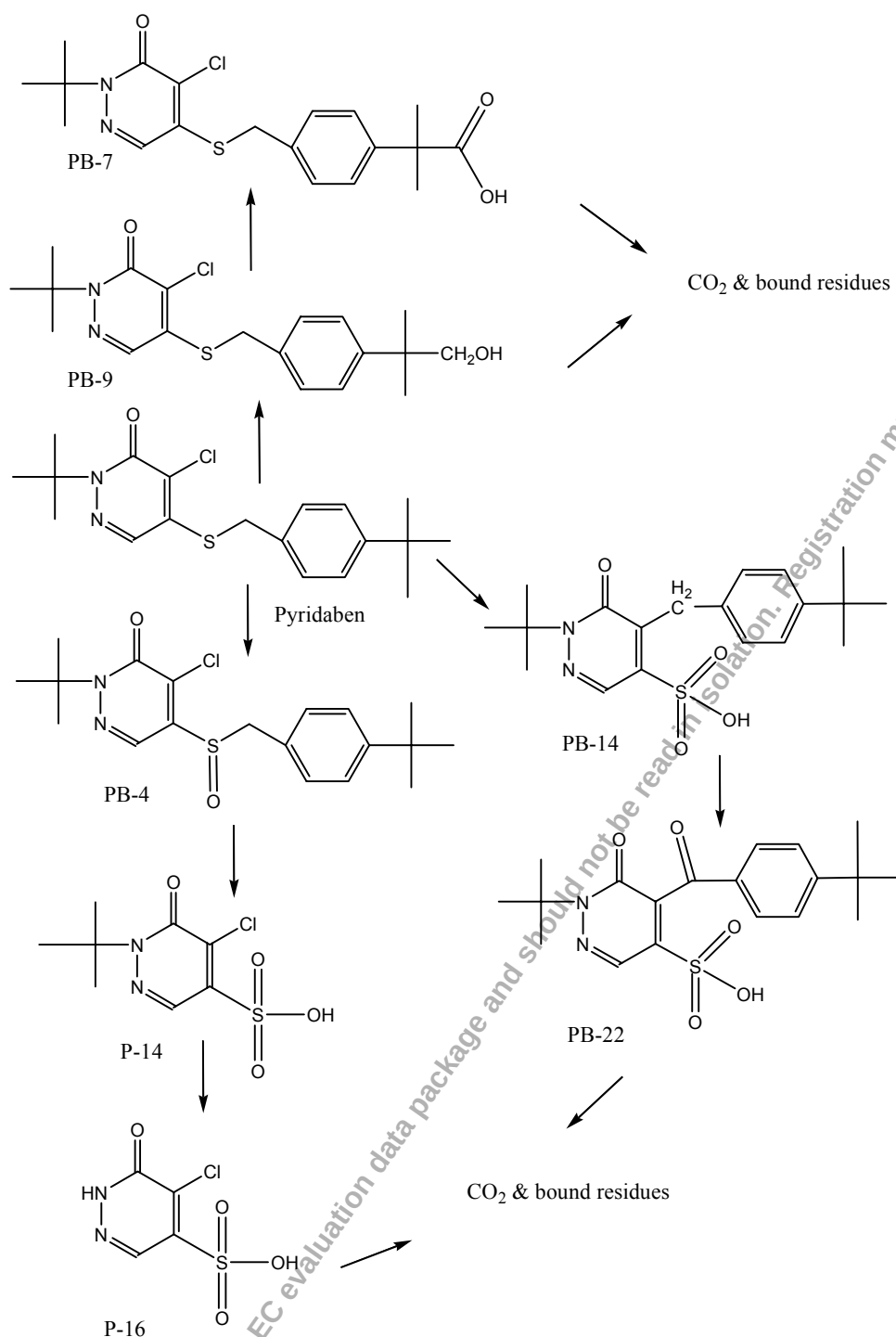


Figure 2.5.2-01 Aerobic metabolic pathway of pyridaben in soil

Anaerobic degradation

No acceptable data on anaerobic degradation of pyridaben in soil were submitted. This information is not required because anaerobic conditions in soil treated with pyridaben are not anticipated, considering the proposed use pattern (greenhouse application and treatment of citrus).

Soil photolysis

Degradation of pyridaben in irradiated soil (≥ 290 nm & 425 W/m^2 , 12 hour dark-light cycles: DT₅₀ 11 days) was faster than in dark soil (DT₅₀ 50 days). The metabolite PB-22 was not detected in dark soil, but found at levels up to 13% AR in irradiated samples, and requires therefore further consideration.

Field dissipation trials

Following single treatment of bare soil at two locations in Denmark (trial 1 & 2) and two in Spain (trial 3 & 4), with a spring application for trials 1-3 (nominal dose 250 g a.s./ha) or an autumn application (nominal dose 300 g a.s./ha) for trial 4, residues of pyridaben were confined to the 0-10 cm segment and dissipated in trials 1, 2, 3 and 4, respectively, with DT₅₀ values of 31, 36, 5.0 and 128 days and DT₉₀ values of 186, 160, 98 and 424 days.

Data requirements

DT₅₀ values in three soils are required for the metabolites PB-4 and PB-7 and the photodegrade PB-22.

PECsoil estimations

Authorisation is requested for treatment of tomato (under glass) involving one application at 0.25 kg a.s./ha (Northern and Southern Europe, cGAP). Calculations were performed according to the methods outlined in 7617/VI/96 "Soil persistence models and EU registration" and Sanco/10058/2005 vs. 1 March 2005 "FOCUS degradation kinetics". Initial PEC_s values were calculated under the following assumptions: 80% crop interception (i.e. application at BBCH 40-89 in tomato); homogeneous distribution in the top 5 cm layer and a soil bulk density of 1.5 g/cm^3 . The requested application on citrus (Southern Europe only) involves a single application of 0.3 kg a.s./ha. For this application, initial PEC_s values were calculated under the following assumptions: 70% crop interception (all growth stages); homogeneous distribution in the top 5 cm layer and a soil bulk density of 1.5 g/cm^3 .

In the soil metabolism studies no metabolites >10% AR were observed.

Time weighted average (TWA) PECs values for pyridaben were based on the worst case DT₅₀ (field) value. The worst-case DT₅₀ (field) value was 36 days for Europe-N (obtained by DFOP; $g = 0.515924$, $k_1 = 0.435319$, $k_2 = 0.00985516$) and 128 days for Europe-S (obtained by SFO; $k_p = 0.00543386$).

For Europe-N, soil concentrations (at time t) were calculated as $PEC_t = PIEC \times (g \exp(-k_1 t) + (1-g) \exp(-k_2 t))$

TWA PECs values were using the formula below:

$$PEC_{S,twa} = (PEC_{S,0}/t) \{ (g/k_1)[1 - \exp(-k_1 t)] + [(1-g)/k_2][1 - \exp(-k_2 t)] \}$$

For Europe-S, TWA PECs values for Southern Europe were calculated according to the formula:

$$PEC_{twa} = PEC_i \cdot (1 - e^{-k \cdot t}) / (k \cdot t), \text{ where:}$$

PEC_i is the initial PEC_S value;

$$k = \ln(2)/DT_{50};$$

t is the time period.

Table 2.5.2-03 presents the substance parameters used for the calculations.

Table 2.5.2-03 Substance parameters used for PECs estimations.

Parameter	pyridaben
max. DT_{50} field (d)	36 (Europe-N) and 128 (Europe-S)
Kinetic model	FOMC
Model parameter α	0.5778833
Model parameter β	86.2897

Under the above assumptions, application of pyridaben (applied as a 75WP formulation according to the cGAP) will lead to the PECs values in Table 2.5.2-04&-05 (Tomatoes) and 2.5.2-06 (Citrus).

Table 2.5.2-04 Actual and TWA PECs (mg/kg) of pyridaben following application in tomato according to the cGAP in Northern Europe (1 x 0.25 kg a.s./ha).

days after treatment	Pyridaben	
	actual	TWA
0	0.067	-
1	0.054	0.060
2	0.046	0.055
4	0.037	0.048
7	0.032	0.042
21	0.026	0.033
28	0.024	0.031
50	0.020	0.027
100	0.012	0.021

Table 2.5.2-05 Actual and TWA PECs (mg/kg) of pyridaben following application in tomato according to the cGAP in Southern Europe (1 x 0.25 kg a.s./ha).

days after treatment	Pyridaben	
	actual	TWA
0	0.067	-
1	0.066	0.066
2	0.066	0.066
4	0.065	0.066
7	0.064	0.065
21	0.060	0.063
28	0.057	0.062
50	0.051	0.058
100	0.039	0.051

Table 2.5.2-06 Actual and TWA PECs (mg/kg) of pyridaben following application in citrus according to the cGAP in Southern Europe (1 x 0.3 kg a.s./ha).

days after treatment	Pyridaben	
	actual	TWA
0	0.120	-
1	0.119	0.120
2	0.119	0.119
4	0.117	0.119
7	0.116	0.118
21	0.107	0.113
28	0.103	0.111
50	0.092	0.105
100	0.070	0.093

The worst-case $DT_{50\text{lab}}$ (20°C) for pyridaben is 199 days, and thus exceeds 60 days. The worst-case $DT_{50\text{field}}$ and $DT_{90\text{field}}$ for pyridaben (Southern Europe) were 128 and 424 days (SFO) and exceed 3 months and 1 year, respectively. Therefore, accumulation was calculated for pyridaben using the worst-case $DT_{50\text{field}}$ (128 d) and SFO kinetics. Average and maximum plateau values were calculated for pyridaben after yearly applications in tomato and citrus (according to the methods outlined in 7617/VI/96 "Soil persistence models and EU registration").

The time course of the pyridaben concentrations and plateau maximums in soil following ten yearly applications of pyridaben in tomato and citrus is illustrated in Figures 2.5.2-02 and 2.5.2-03. The actual, TWA, plateau maximum and plateau average concentrations are given in Table 2.5.2-07.

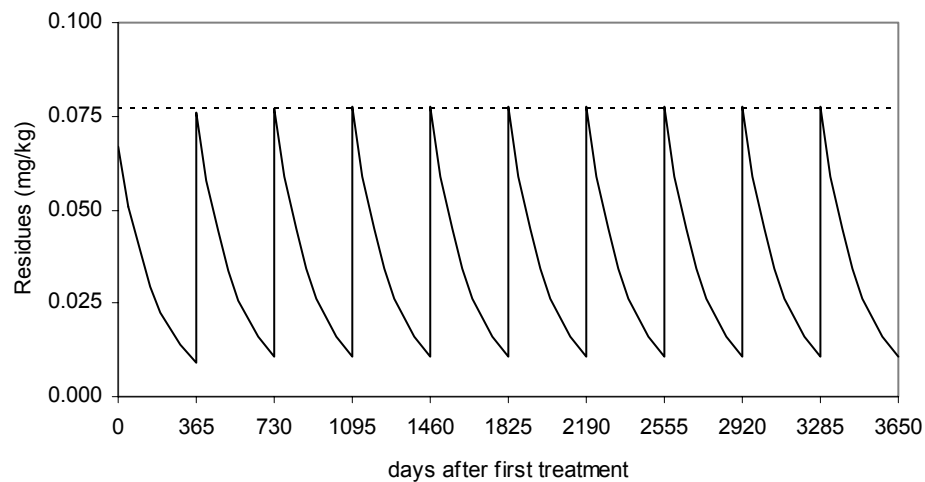


Figure 2.5.2-02 Accumulation of pyridaben in soil after yearly applications of pyridaben in tomato.

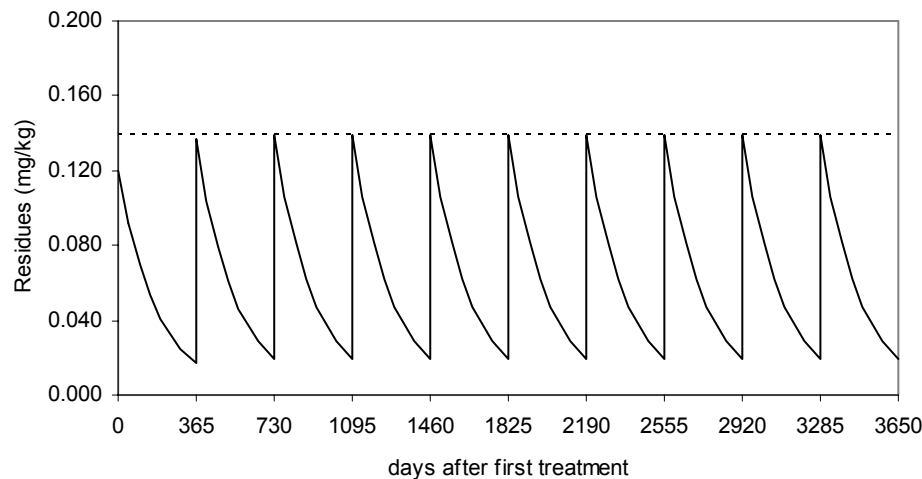


Figure 2.5.2-03 Accumulation of pyridaben in soil (Southern Europe) after yearly applications of pyridaben in citrus.

Table 2.5.2-07 Actual and TWA PECs (mg/kg) of pyridaben following the plateau maximum reached after 10 yearly pyridaben applications in tomato (Northern and Southern Europe) and citrus (Southern Europe).

Time after last application (days)	Tomato		Citrus	
	actual	TWA	actual	TWA
1	0.077	0.077	0.139	0.139
2	0.077	0.077	0.138	0.139
4	0.076	0.077	0.136	0.138
7	0.075	0.076	0.134	0.137
21	0.069	0.073	0.124	0.132
28	0.067	0.072	0.120	0.129
50	0.059	0.068	0.106	0.122
100	0.045	0.060	0.081	0.108
plateau maximum	0.077		0.139	
average plateau conc.	0.034		0.061	
plateau reached after	2 years (on the day of the 3 rd annual application)		2 years (on the day of the 3 rd annual application)	

Batch sorption

Table 2.5.2-08 presents a summary of the adsorption coefficients of pyridaben determined in batch sorption studies with 4 soils (pH 5.2-7.3, 0.25-0.69% organic carbon) at 25°C and a soil:water ratio of 1:20 or 1:40.

Table 2.5.2-08 Adsorption coefficients of pyridaben from batch sorption studies

substance	Soil	pH	% oc	CEC (meq/100 g)	% clay	% smectite	K _F (L/kg)	1/n	K _{Foc} (L/kg)
Pyridaben	sandy loam	7.3	0.31	8.2	7	0.21	108	0.92	34858
	silt loam	7.0	0.42	23.2	13	1.04	330	1.03	78683
	silt loam	5.2	0.25	4.1	15	3.45	220	0.96	87918
	sand	5.5	0.69	3.2	4	1.72	445	0.90	64551
	mean							0.953	66503

The K_F value for the fifth tested soil, a clay loam, was 6659 L/kg (1/n = 1.28), and sorption was much higher than expected on the basis of its organic carbon content (0.31%). The high sorption in the clay loam soil may be explained by the high clay and in particular smectite content, and therefore no K_{oc} was calculated. No pH dependency of adsorption was observed.

Estimation methods

For the soil metabolite PB-4 a K_{oc} value of 71490 L/kg is available, which was estimated by the computer programme Syracuse (EPIWIN).

Non-aged column leaching

Data were not submitted and are not required.

Aged column leaching

Data were not submitted and are not required.

PECgw estimations

PEC_{gw} were estimated using FOCUS-PEARL version 2.2.2. Model input was based on the recommendations in "FOCUS groundwater scenarios in the EU review of active substances" Sanco/321/2000 rev.2 and "Generic guidance for FOCUS groundwater scenarios" version 1.1 of April 2002. For citrus, annual applications were simulated for a period of 20 years with a six year "warm-up period". Simulations were performed for the Piacenza, Porto, Thiva and Sevilla FOCUS scenarios (the only scenarios applicable to citrus). Because no application dates were specified by the notifier, calculations were performed for applications in January, April and October to simulate year-round use. For tomato, no FOCUS calculations were performed because all uses for which authorisation is requested are in greenhouses (for which no FOCUS scenario is applicable). Instead, for tomato, PEC_{gw} values of pyridaben and PB-4 were estimated using the standard Dutch spring scenario as defined in PEARL version 2.2.2 for a dose of 1 kg/ha for each compound.

PECgw were estimated for pyridaben and for PB-4. PECgw calculations could not be performed for the soil metabolite PB-7 (exceeding $2 \times 5\%$ at two consecutive time points in laboratory soil degradation studies) and the soil photodegradate PB-22. Since for these two compounds no reliable Koc values were available, worst case modelling might be performed using $K_{oc} = 0$ L/kg. Since however no DT50 values were available for PB-7 and PB-22, PECgw calculations were not made for these compounds.

In all citrus scenarios, estimated 80th percentile concentrations in groundwater were <0.001 µg/L for pyridaben and PB-4, and the groundwater trigger of 0.1 µg/L was not exceeded. The maximum average substance concentrations in the upper groundwater, calculated using the standard DUTCH spring application scenario (representative for greenhouse application of tomato), were <0.001 µg/L for pyridaben and metabolite PB-4.

Data requirements

Koc values in three soils are required for the soil metabolite PB-7 and for the soil photodegradate PB-22.

2.5.3 Fate and behaviour in water

Hydrolysis

No hydrolytic degradation of pyridaben was observed after 30 days incubation at pH 5.0, pH 7.0 and pH 9.0 and 25°C.

Photolysis

The DT50 for aquatic photolysis of pyridaben at 25°C (Xenon light, 425 W/m²) is 6.8 minutes. Major photodegradates were W-1 (max. 27.9% AR, DT50 <1.5 hours) and B-3 (max. 29.2% AR, photolytically stable). The structures of these two compounds are shown in Figure 2.5.3-01. The quantum yield of pyridaben at 20°C was 0.0304 mole/Einstein.

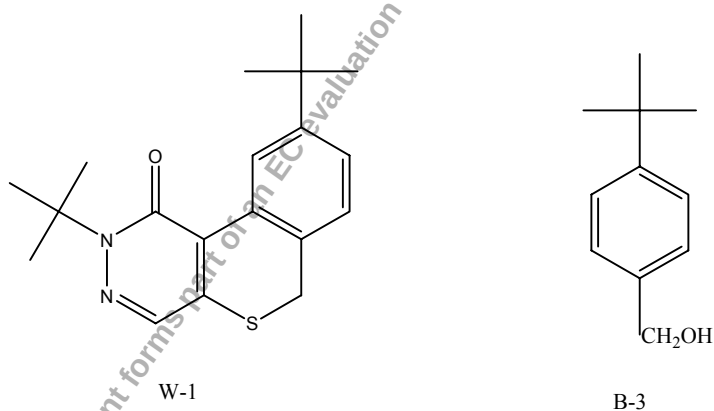


Figure 2.5.3-01 Aqueous photodegradates of pyridaben detected at $>10\%$ AR

Biodegradability

Ready biodegradability

Pyridaben was not readily biodegradable in a modified Sturm test.

Aerobic water/sediment studies

In two water/sediment systems, treated with [benzene-U-14C]-pyridaben or [pyridazinone-3,6-14C]-pyridaben at a concentration of 12 µg/L and incubated at 20°C in the dark for 120 days, pyridaben degraded in the total water/sediment system with half-lives of 7.0-31 days (persistence) and 39-651 days (modelling). The levels of parent pyridaben reached a maximum in sediment of 41-55% AR on day 2-14, and pyridaben dissipated from the sediment with persistence half-lives of 49-207 days, and from the water phase with persistence half-lives of 0.4-7.7 days. The non-extractable fraction in sediment increased to a maximum of 38-47% AR on day 59-120, and CO₂ to 0.1-6.2% AR on day 120. The main metabolite was PB-7, which reached maximum levels in water and sediment of 5.8-17% AR and 11-14% AR respectively. No other metabolites were found at >10% AR in water or sediment.

The (persistence) half-lives of pyridaben are listed in Table 2.5.3-01. DT₅₀ values for modelling are listed in Table 2.5.3-02. No DT50 values could be evaluated for the major water/sediment metabolite PB-7.

Table 2.5.3-01 Persistence DT50 and DT90 values (20°C) of pyridaben in water-sediment systems.

Compound	system	14C-label	DT ₅₀			DT ₉₀		
			water ¹	sediment ¹	total ²	water ¹	sediment ¹	total ²
Pyridaben	silty clay	Pyr	7.7 ³	49.4 ⁵	28.8 ⁵	25.4 ³	1245 ⁵	985 ⁵
		Ben	0.39 ⁴	51.7 ³	31.1 ⁶	16.2 ⁴	172 ³	210 ⁶
	sandy silt loam	Pyr	1.3 ⁴	207 ⁵	7.0 ⁶	4.9 ⁴	2340 ⁵	3769 ⁶
		Ben	0.49 ⁶	118 ³	14.9 ⁴	4.9 ⁶	392 ³	278 ⁴
	mean		2.5	107	20.5	12.9	1037	1311

¹ half-lives for dissipation

² half-lives for degradation

³ based on SFO model (Single First-Order)

⁴ based on DFOP model (Dual First-Order-in-Parallel)

⁵ based on HS model (Hockey Stick)

⁶ based on FOMC model (First-Order-Multi-Compartment)

Table 2.5.3-02 Modelling DT50 and DT90 values (20°C) of pyridaben in water-sediment systems.

compound	system	14C-label	DT50 (system) ¹
Pyridaben	silty clay	Pyr	651 ⁴
		Ben	38.9 ²
	sandy silt loam	Pyr	72.0 ³
		Ben	113 ³
	mean		219

¹ half-life for degradation² based on SFO model (Single First-Order)³ based on DFOP model (Dual First-Order-in-Parallel)⁴ based on HS model (Hockey Stick)Anaerobic water/sediment studies

No studies were submitted. These studies are not required.

The main transformations of pyridaben in water-sediment systems are shown in Figure 2.5.3-02.

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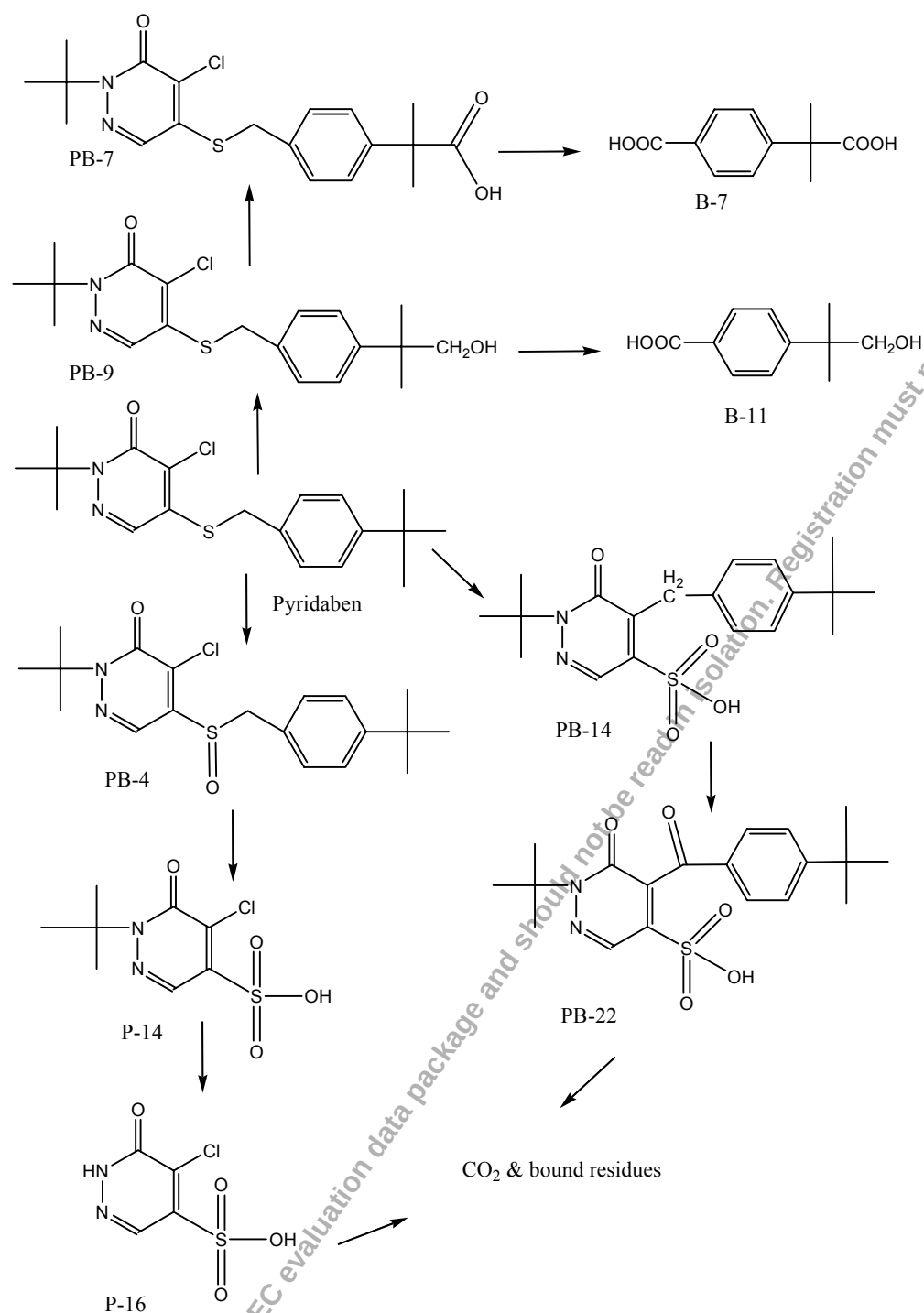


Figure 2.5.3-02 Main transformations of pyridaben in water-sediment systems

Data requirements

None.

PEC_{sw} estimations

Application to tomato

Predicted environmental concentrations in surface water (PEC_{sw}) of pyridaben were calculated according STEP 2 procedures outlined in Sanco/4802/2001 rev.2 final (May 2003) "FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC" using FOCUS 1-2 software, version 1.1 (STEP 1 calculations were not performed because the STEP 1 default scenario is not applicable for greenhouse applications). In order to mimic a greenhouse application, inputs through runoff and drainage were set equal to zero. For soil, the geometric mean soil DT_{50,lab} (132.6 days, modelling endpoint, 20°C, corrected for moisture content) and K_{om} were used in agreement with the guidance (Sanco/10058/2005 vs 1.0 March 2005 and Sanco/4802/2001). During the evaluation process, one of the soil DT₅₀ values was changed from 1104 days (DFOP fit) to 95 days (SFO fit), leading to a new geomean DT₅₀ value of 71.8 days. The PEC values for surface water and sediment were already calculated with the conservative soil DT₅₀ endpoint. The presented values can therefore be considered as worst-case. For water and sediment, no individual DT₅₀ values are available. Therefore the arithmetic mean of the available DT₅₀ values for the whole water/sediment system was used for both water and sediment in agreement with the guidance (Sanco/4802/2001).

The proposed use on tomato involves a greenhouse application with limited exposure of surface water. A total surface water loading of 0.1% of the dose is assumed (the value of 0.1% emission is used in The Netherlands for greenhouse applications). STEP 2 calculations have a default drift value of 2.759% (single application). Therefore, the STEP 2 results were divided by a factor 27.59 to obtain PEC_{sw} and PEC_{sed} concentrations relevant for a total assumed loading of 0.1% of the dose for greenhouse applications.

In the water/sediment studies, one major metabolite (PB-7) was observed (max 29% AR in total system, max 17% AR in water and max 14% AR in sediment). Because no half-lives for PB-7 could be calculated, no PEC_{sw} calculations according to the above methods were performed. A rough indication of the maximum concentration can be obtained by multiplying the T=0 result for pyridaben with the maximum % of occurrence of PB-7 in water or sediment and by applying a MW correction factor of 1.08 (i.e. 394.9/364.9).

Similar to PB-7, because no half-lives for W-1 and B-3 are available, no PEC_{sw} calculations according to the above methods were performed. A rough indication of the maximum concentration can be obtained by multiplying the T=0 result for pyridaben with the maximum % of occurrence of W-1 or B-3 in water or sediment and by applying a MW correction factor of 0.90 (i.e. 328.5/364.9) for W-1 and of 0.45 for B-3 (i.e. 164.3/364.9). As worst-case approach, the maximum % of occurrence of W-1 and B-3 in the aqueous photolysis study was either completely attributed to the water or to the sediment phase.

STEP 2:

The following substance specific input data were used to run the model:

Application rate:	250 g ai/ha (cGAP for greenhouse applications)
Application/crop type:	vegetables, fruiting
Application number:	1
Application interval:	not applicable
Water solubility:	Pyridaben: 0.012 mg/L (24°C).
K _{OC} :	Pyridaben: 66503 L/kg.
DT ₅₀ water/sediment:	Pyridaben: 218.7 d (arithmetic mean, modelling endpoint).
DT ₅₀ water:	Values for total system were used.
DT ₅₀ sediment:	Values for total system were used.
DT ₅₀ soil: Pyridaben:	132.6 d (geometric mean, modelling endpoint).

Besides the data presented above the following additional information is considered in STEP 2:

Region and season of application:	No Runoff/Drainage
Crop interception:	Average crop cover (i.e. 50% interception)

The default model data selection in STEP 2 used for the calculations is:

Distance to water body:	1 m
Spray drift (multiple application):	2.759% (note: STEP 2 results were divided by a factor 27.59 to simulate a loading of 0.1%)
Ratio of field to water body:	10 : 1
Water depth:	30 cm
Sediment depth:	5 cm
Effective sediment for sorption:	1 cm
Sediment organic carbon:	5 %
Sediment bulk density:	0.8 kg/L

Under the above assumptions, application of pyridaben formulated as 75WP on tomato in greenhouses according to cGAP (1 x 0.25 kg a.s./ha; cGAP) will lead to PEC_{sw} values of pyridaben and PB-7 listed in Table 2.5.3-03, -04, -05 & -06.

Table 2.5.3-03 Calculated pyridaben concentrations in water and sediment (STEP 2) for application on tomato (1 x 0.25 kg a.s./ha; cGAP)

Time (d)	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.0833	-	0.6026	-
1	0.0283	0.0558	0.6023	0.6024
2	0.0102	0.0375	0.6009	0.6020
4	0.0023	0.0214	0.5973	0.6005
7	0.0014	0.0129	0.5917	0.5979
14	0.0013	0.0071	0.5787	0.5916
21	0.0013	0.0052	0.5660	0.5851
28	0.0013	0.0042	0.5536	0.5788
42	0.0012	0.0032	0.5295	0.5664
50	0.0012	0.0029	0.5163	0.5594
100	0.0010	0.0020	0.4406	0.5184

Table 2.5.3-04 Calculated PB-7 concentrations in water and sediment (STEP 2) for application on tomato (1 x 0.25 kg a.s./ha; cGAP)

Time (d)	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.0153	-	0.0913	-

water: calculated as PEC_{sw} pyridaben x 0.17 x 1.08

sediment: calculated as PEC_{sed} pyridaben x 0.14 x 1.08

Table 2.5.3-05 Calculated W-1 concentrations in water and sediment (STEP 2) for application on tomato (1 x 0.25 kg a.s./ha; cGAP)

Time (d)	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.0209	-	0.1513	-

water: calculated as PEC_{sw} pyridaben x 0.279 x 0.90

sediment: calculated as PEC_{sed} pyridaben x 0.279 x 0.90

Table 2.5.3-06 Calculated B-3 concentrations in water and sediment (STEP 2) for application on tomato (1 x 0.25 kg a.s./ha; cGAP)

Time (d)	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.0109	-	0.0792	-

water: calculated as PEC_{sw} pyridaben x 0.292 x 0.45

sediment: calculated as PEC_{sed} pyridaben x 0.292 x 0.45

Application on citrus

Predicted environmental concentrations in surface water (PEC_{sw}) of pyridaben were calculated according STEP 1 and STEP 2 procedures outlined in Sanco/4802/2001 rev.2 final (May 2003) "FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC" using FOCUS 1-2 software, version 1.1. The appropriate (worst case) standard scenarios were used for the

calculations for applications on citrus. For soil, the geometric mean soil $DT_{50,lab}$ (modelling endpoint, 20°C, corrected for moisture content) and K_{om} was used in agreement with the guidance (Sanco/10058/2005 version 1.0 March 2005 and Sanco/4802/2001). For water and sediment, no individual DT_{50} values are available. Therefore the arithmetic mean of the available DT_{50} values for the whole water/sediment system was used for both water and sediment in agreement with the guidance (Sanco/4802/2001).

STEP 1:

The following substance specific input data were used to run the first tier of the model:

Application rate:	300 g ai/ha
Application type:	citrus
Application number:	1
Water solubility:	See above (tomato)
K_{oc} :	See above (tomato)
DT_{50} water/sediment:	See above (tomato)

The default model data selection in STEP 1 used for the calculations is:

Distance to water body:	1 m
Spray drift	15.725%
Runoff + drainage:	10% (of applied amount)
Ratio of field to water body:	10 : 1
Water depth:	30 cm
Sediment depth:	5 cm
Effective sediment for sorption:	1 cm
Sediment organic carbon:	5 %
Sediment bulk density:	0.8 kg/L

STEP 2:

Besides the data presented above the following additional information is considered in STEP 2:

Region and season of application:	Southern Europe, June-Sep, Mar-May and Oct-Feb (according to cGAP)
Crop interception:	Average canopy (i.e. 70% interception)
DT ₅₀ water:	Values for total system were used (see tomato)
DT ₅₀ sediment:	Values for total system were used (see tomato)
DT ₅₀ soil:	See above (tomato)

The model data selection on STEP 2 differs then as compared to STEP 1 as follows:

Runoff + drainage: 3% (June-Sep) or 4% (Mar-May and Oct-Feb)

STEP 1 and STEP 2 calculations resulted in PEC_{sw} concentrations of pyridaben (15.7-16.8 µg/L) exceeding the water solubility of 12 µg/L. Therefore STEP 3 calculations were performed for pyridaben.

In the water/sediment studies, one major metabolite (PB-7) was observed (max 29% AR in total system, max 17% AR in water and max 14% AR in sediment). Because no half-lives for PB-7 could be calculated, no PEC_{sw} calculations were performed according to the above methods. A rough indication of the maximum concentration can be obtained by multiplying the T=0 results for pyridaben (STEP 1) with the maximum % of occurrence of PB-7 in water or sediment and by applying a MW correction factor of 1.08 (i.e. 394.9/364.9) (Table 2.5.3-07).

Similar to PB-7, because no half-lives for W-1 and B-3 are available, no PEC_{sw} calculations according to the above methods were performed. A rough indication of the maximum concentration can be obtained by multiplying the T=0 result for pyridaben with the maximum % of occurrence of W-1 or B-3 in water or sediment and by applying a MW correction factor of 0.90 (i.e. 328.5/364.9) for W-1 and of 0.45 for B-3 (i.e. 164.3/364.9). As worst-case approach, the maximum % of occurrence of W-1 and B-3 in the aqueous photolysis study was either completely attributed to the water or to the sediment phase (Table 2.5.3-08 and -09).

Table 2.5.3-07 Calculated PB-7 concentrations in water and sediment (STEP 1) for application on citrus (1 x 0.3 kg a.s./ha; cGAP)

Time (d)	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	3.0982	-	112.3653	-

water: calculated as STEP 1 PEC_{sw} pyridaben (16.8402) x 0.17 x 1.08

sediment: calculated as STEP 1 PEC_{sed} pyridaben (741.6361) x 0.14 x 1.08

Table 2.5.3-08 Calculated W-1 concentrations in water and sediment (STEP 1) for application on citrus (1 x 0.3 kg a.s./ha; cGAP)

Time (d)	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	4.2286	-	186.2248	-

water: calculated as STEP 1 PEC_{sw} pyridaben (16.8402) x 0.279 x 0.90

sediment: calculated as STEP 1 PEC_{sed} pyridaben (741.6361) x 0.279 x 0.90

Table 2.5.3-09 Calculated B-3 concentrations in water and sediment (STEP 1) for application on citrus (1 x 0.3 kg a.s./ha; cGAP)

Time (d)	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	2.2128	-	97.4510	-

water: calculated as STEP 1 PEC_{sw} pyridaben (16.8402) x 0.292 x 0.45

sediment: calculated as STEP 1 PEC_{sed} pyridaben (741.6361) x 0.292 x 0.45

STEP 3:

FOCUS STEP 3 calculations were performed by the RMS for pyridaben according to the procedures outlined in Sanco/4802/2001 rev.2 final (May 2003) "FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC" using the SWASH software tool, version 2.1. The FOCUS wizard was used to generate all relevant crop-scenario combinations for citrus (according to FOCUS, only the D6 ditch and R4 stream scenario is applicable to citrus). Because no application dates were specified by the notifier, several application windows were assessed: January, May and October. These windows encompass winter, spring and fall applications and can be considered representative for year-round use. The substance data were the same as used for the STEP 1-2 calculations, with following additions: vapour pressure 1E-5 Pa (40°C) and arithmetic mean Freundlich 1/n value 0.953. The vapour pressure was determined at 52.7°C, however FOCUS does not allow values >40°C, hence 40°C was used as temperature. All other input parameters were set at the default FOCUS values. Pyridaben inputs in surface water via drainage were calculated using MACRO in FOCUS software version 4.3b and via run-off by PRZM in FOCUS version 3.21.b. PEC_{sw} values were obtained using TOXSWA in FOCUS software version 2.1.1.F1.

The STEP 3 pyridaben PEC_{sw} and PEC_{sed} concentrations and the time weighted average PEC_{sw} and PEC_{sed} concentrations after application on citrus according to the cGAP are presented in Table 2.5.3-10 and 2.5.3-11.

Table 2.5.3-10 Calculated pyridaben concentrations in water and sediment (STEP 3, D6 ditch and R4 stream scenario) for application on citrus

Scenario	Time	Jan		May		Oct	
		PEC _{sw} (µg/L)	PEC _{sed} (µg/kg)	PEC _{sw} (µg/L)	PEC _{sed} (µg/kg)	PEC _{sw} (µg/L)	PEC _{sed} (µg/kg)
D6 ditch	0	10.402	58.824	10.402	57.757	10.402	57.910
	1	5.207	58.694	5.187	57.613	5.190	57.771
	2	4.192	58.353	4.162	57.241	4.166	57.405
	4	3.204	57.251	3.163	56.047	3.169	56.227
	7	2.356	55.068	2.307	53.694	2.314	53.900
	14	1.257	49.652	1.213	47.893	1.219	48.153
	21	0.761	44.975	0.725	42.905	0.730	43.209
	28	0.512	35.677	0.483	38.554	0.487	39.372
	42	0.019	27.860	0.255	32.015	0.267	33.713
	50	0.027	25.679	0.191	29.166	0.204	31.244
	100	0.046	18.448	0.054	17.896	0.067	22.199
R4 stream	0	7.820	15.982	7.736	11.320	7.165	14.784
	1	0.018	6.903	0.011	3.091	0.001	14.316
	2	0.006	5.803	0.003	2.233	0.000	14.147
	4	0.002	4.998	0.001	1.603	0.000	13.928
	7	0.001	4.505	0.000	1.221	0.000	13.740
	14	0.000	4.029	0.065	2.525	0.001	13.421
	21	0.000	3.798	0.000	5.564	0.000	13.172
	28	0.000	3.646	0.000	5.285	0.000	12.955
	42	0.000	3.426	0.000	4.873	0.000	12.586
	50	0.000	3.332	0.000	4.689	0.000	12.401
	100	0.000	3.349	0.000	3.735	0.000	11.448

Note: calculated maximum values in bold.

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Table 2.5.3-11 Calculated pyridaben TWA concentrations in water and sediment (STEP 3, D6 ditch and R4 stream scenario) for application on citrus

Scenario	Time	Jan		May		Oct	
		TWA PEC _{sw} (µg/L)	TWA PEC _{sed} (µg/kg)	TWA PEC _{sw} (µg/L)	TWA PEC _{sed} (µg/kg)	TWA PEC _{sw} (µg/L)	TWA PEC _{sed} (µg/kg)
D6 ditch	0	-	-	-	-	-	-
	1	6.482	58.812	6.470	57.744	6.472	57.897
	2	5.577	58.777	5.558	57.706	5.561	57.859
	4	4.616	58.637	4.589	57.555	4.593	57.710
	7	3.820	58.269	3.785	57.154	3.790	57.314
	14	2.779	56.829	2.737	55.595	2.743	55.772
	21	2.179	54.929	2.138	53.540	2.144	53.740
	28	1.791	52.894	1.752	51.346	1.757	51.568
	42	1.237	47.590	1.285	47.092	1.292	47.510
	50	1.042	44.676	1.115	44.890	1.122	45.482
	100	0.547	33.822	0.609	34.750	0.619	36.529
R4 stream	0	-	-	-	-	-	-
	1	1.102	9.962	0.883	8.574	0.331	14.506
	2	0.556	8.183	0.445	8.530	0.166	14.376
	4	0.280	6.784	0.223	8.476	0.086	14.211
	7	0.160	6.114	0.128	8.424	0.052	14.052
	14	0.080	6.009	0.069	8.350	0.037	13.817
	21	0.054	5.931	0.052	8.339	0.027	13.645
	28	0.040	5.861	0.039	8.301	0.021	13.502
	42	0.027	5.782	0.026	8.215	0.014	13.259
	50	0.023	5.777	0.022	8.167	0.012	13.138
	100	0.013	5.511	0.011	7.850	0.006	12.528

Note: calculated maximum TWA₂₈ values in bold.

Predicted concentrations in sediment

For calculations of concentrations of pyridaben and metabolites in aqueous sediment after application of pyridaben formulated as 75WP in tomato and citrus, see above PEC_{sw} estimations.

2.5.4 Fate and behaviour in air

Pyridaben

Based on a vapour pressure of 1×10^{-5} Pa at 24°C (Volume 3, section B.2) and a water solubility of 0.012 mg/L at 24°C, the calculated Henry's Law Constant of pyridaben at 24°C was $0.304 \text{ Pa} \cdot \text{m}^3 \cdot \text{mol}^{-1}$ (Volume 3, section B.2). Results for photochemical oxidative degradation of pyridaben (DT_{50} 4.8 hrs) and the Henry's Law constant of $0.304 \text{ Pa} \cdot \text{m}^3 \cdot \text{mol}^{-1}$ suggest that the concentrations of pyridaben in air are likely to be negligible.

Metabolites PB-22, PB-7, B-3

The vapour pressure, water solubility, Henry's law constant and the atmospheric half-life for the three metabolites were calculated by the Notifier using the models EPISUITE programme and AOPWIN:

- Vapour pressure : PB-22: 6.3E-13 Pa; B-3: 0.157 Pa; PB-7: 2.87E-9 Pa
- Water solubility at 25°C : PB-22: 166.8 mg/l; B-3: 97.8 mg/l; PB-7: 1.65 mg/l
- Henry's law constant : PB-22: 1.5×10^{-17} atm-m³/mol; B-3: 4.3×10^{-7} atm-m³/mol; PB-7: 6.8×10^{-12} atm-m³/mol
- Atmospheric oxidation half-life : PB-22: 1.0 days; B-3: 1.1 days; PB-7: 7.0 days

It can be concluded that based on the physical-chemical properties (i.e. very low vapour pressure, relatively high water solubility, and Henry's law constant) of these metabolites an exposure to air is very unlikely to occur. In addition, the metabolites PB-22 and B-3 would undergo a very fast degradation when entering the atmosphere.

Data requirements

None.

2.6 Effects on non-target species

2.6.1 Effects on terrestrial vertebrates

For the application in tomato (glass house), the routes of exposure to birds and mammals are considered to be:

- consumption of surface water containing residues of pyridaben (acute);
- consumption of fish contaminated with residues of pyridaben (long-term).

For the application in citrus, the routes of exposure to birds and mammals are considered to be:

- consumption of oversprayed insects with residues of pyridaben (short- and long-term);
- consumption of drinking water (surface water and puddles) containing residues of pyridaben (acute);
- consumption of fish contaminated with residues of pyridaben (long-term);
- consumption of earthworms contaminated with residues of pyridaben (long-term).

2.6.1.1 Birds

Avian toxicity data

Acute oral toxicity studies on two species were supplied. The acute LD50-values of pyridaben for bobwhite quail and mallard duck were >2250 and >2500 mg a.s./kg body weight, respectively.

Short-term dietary toxicity studies with pyridaben on two species were supplied. For bobwhite quail and mallard duck, the dietary LC50-values were >5620 and 4688 mg a.s./kg diet. The dietary LC50-value for bobwhite quail was equivalent to >4298 mg a.s./kg bw/day, while an LC50-value expressed as mg a.s./kg bw/day could not be determined for mallard duck. For the latter species, the NOEC for mortality was 3160 mg a.s./kg diet, equivalent to 659 mg a.s./kg bw/day (value to be used in risk assessment).

Reproductive toxicity studies with pyridaben in bobwhite quail and mallard duck were submitted, in which there were no effects on reproductive parameters at 1000 and 100 mg a.s./kg diet, equivalent to 135 and 10 mg a.s./kg bw/day (males) and 130 and 11 mg a.s./kg bw/day (females), respectively.

Risk assessment (active substance)

The acute risk assessment is based on an insectivorous bird of body weight (BW) 10 g feeding exclusively on insects, with a Food Intake Ratio (FIR) of 10.4 g fresh material/day, and a daily water intake (DWI) of 2.7 mL/day. The PEC_{sw} is the worst-case initial PEC_{sw} value (FOCUS Step 2, Northern and Southern Europe for tomato; FOCUS Step 3, Southern Europe for citrus, D6 ditch scenario). Residue values in food and water, ETE and TER_a values are presented in the table below.

Table 2.6.1.1-01 Toxicity Exposure Ratios for exposure of birds to pyridaben due to consumption of contaminated insects and drinking water

appln. kg a.s./ha	Time scale	Toxicity endpoint (mg a.s./kg bw or mg a.s./kg bw/day)	route	PEC _{FEED} or PEC _{WATER} (mg/kg ww or mg/L)	ETE (mg/kg bw/d)	TER
Tomato EU N&S	Acute	>2250	Surface water	8E-05	2E-05	1E+08
Citrus EU S	Acute	>2250	Insects	16	16	139
			Surface water	0.010	0.0028	8E+05
			Puddle water	80	21.6	>104
	Short-term	659	Insects	8.7	9.0	73
	Long-term	10	Insects	8.7	9.0	1.1

The risk to birds is considered to be acceptable for the application in tomato (TER value above 10 for acute). The acute and short-term risk to birds is considered to be acceptable for the application in citrus (TER values above 10), but the long-term risk due to consumption of contaminated insects needs to be refined. No information is available on (the time course of) residue levels in insects. The notifier is requested to provide further data for refined risk assessment of long-term exposure of birds to contaminated insects (e.g. measured residues on insects or PT or PD values).

Long-term risk assessment (bioaccumulation and food chain behaviour)

Long-term risk assessment is based on a bird weighing 100 g feeding exclusively on earthworms, with a daily food intake (DFI) of 113 g fresh material/day or on a fish-eating bird weighing 1000 g with a daily food intake (DFI) of 206 g fish/day.

Residue values in earthworms and fish, ETE and TER values are presented in Table 2.6.1.1-02.

Table 2.6.1.1-02 Long-term toxicity Exposure Ratios for exposure of birds to pyridaben due to consumption of contaminated earthworms and fish

appln. kg a.s./ha	Time scale	NOEC (mg/kg bw/d)	Route	PEC _{FEED} (mg/kg wwt)	ETE (mg/kg bw/d)	TER _{It}
Tomato EU N&S	Long-term	10	Fish	<2E-04	<5E-05	>2E+05
Citrus EU S	Long-term	10	Earthworms	>2.0	>2.3	<4.4
			Fish	<0.10	<0.02	>464

The long-term risk to birds as a result of bio-accumulation in fish is considered to be acceptable (TER_{It} above 5). The TER_{It} value for consumption of earthworms is <4.4 and therefore, a risk cannot be excluded. The notifier is requested to provide additional data for a refined risk assessment for this route (e.g. PT or PD values, measured residues in earthworms).

Conclusion:

The acute and short-term risk to birds is considered to be acceptable. The long-term risk to birds due to consumption of contaminated fish is considered to be acceptable, but the long-term risk due to consumption of contaminated insects and earthworms needs to be refined.

Bio-magnification in terrestrial food chains

The bioaccumulation potential reported in the List of Endpoints of the Toxicology section is stated to be low. Hence, according to the guidance provided in SANCO/4145/2000 – final (25 September 2002), the risk for biomagnification in terrestrial food chains is low.

Risk of metabolites for birds

A risk assessment is performed for metabolites formed at a maximum level of at least 10% TRR in plants. In plant metabolism studies, individual identified metabolites were at the most 5.1% TRR in apple fruit (25 days after treatment), 4.6% TRR in citrus fruit (7 days after the second treatment) and 1.1% TRR in tomato fruit (14 days after treatment). Hence no individual identified metabolite exceeded 10% TRR, and no assessment of plant metabolites is made.

Conclusion:

The acute and long-term risk resulting from exposure of birds to the metabolites of pyridaben is low for both applications.

2.6.1.2 Mammals**Risk assessment (active substance)**

The acute risk assessment is based on a herbivorous mammal of body weight (BW) 25 g feeding exclusively on grasses (FIR 34.8 g/day). Assessment of exposure to pyridaben via intake of contaminated surface water however is based on a small mammal weighing 10 g, with a daily water intake (DWI) of 1.6 mL/day.

The risk of bio-accumulation was considered for the routes earthworm and fish. The assessment was based on a mammal weighing 10 g feeding exclusively on earthworms, with a daily food intake (DFI) of 14 g fresh material/day or on a fish-eating mammal weighing 3000 g with a daily food intake (DFI) of 390 g fish/day.

Residue levels in food and water, and ETE and TER values are presented in Table 2.6.1.2-01.

Table 2.6.1.2-01 Toxicity Exposure Ratios for exposure of mammals to pyridaben due to consumption of contaminated grasses, drinking water, earthworms and fish

appln.	Time scale	Toxicity endpoint (mg a.s./kg bw or mg a.s./kg bw/day)	Route	PEC _{FEED} or PEC _{WATER} (mg/kg ww or mg/L)	ETE (mg/kg bw/d)	TER
Tomato EU N&S	Acute	161	surface water	8E-05	1E-05	1E+07
	Long-term	1.87	Fish	<2E-04	<3E-05	>6E+04
Citrus EU S	Acute	161	Grasses	13	18	9.0
		161	Surface water	0.010	0.0016	1E+05
		161	Puddle water	80	12.8	12.6
	Long-term	1.87	Grasses	3.6	5.0	0.37
		1.87	Earthworms	>2.0	>2.8	<0.67
		1.87	Fish	<0.10	<0.014	>138

The acute risk to mammals is considered to be acceptable for consumption of contaminated drinking water (TER above 10). A risk is expected due to consumption of contaminated grass, and therefore, the risk assessment needs to be refined for this route.

The long-term risk due to consumption of contaminated fish is considered to be acceptable (TER above 5). The long-term risk assessment for the routes grasses and earthworms needs to be refined. The notifier is requested to provide further data for refined risk assessment of long-term

exposure of mammals to contaminated grass and earthworms (e.g. PT or PD values, measured residues in grass and earthworms).

Refinement of the acute risk due to consumption of contaminated grasses

The lowest acute oral LD50 in rat was obtained in a study where animals were treated with pyridaben suspended in maize oil (LD50 values 161 and 181 mg/kg bw for males and females respectively). Two other studies were available, where animals were treated with pyridaben suspended in aqueous carboxymethyl cellulose. In this vehicle the toxicity of pyridaben was much lower: LD50 values were 570-820 and 1100-1350 mg/kg bw for males and females respectively. As there appears to be an effect of the vehicle on the toxicity of pyridaben, the most appropriate toxicity value for risk assessment is that determined in a vehicle resembling closely the environmental matrix through which mammals are exposed. The formulation is sprayed in an aqueous solution and grasses are a watery matrix, so the LD50 values determined with pyridaben suspended in aqueous carboxymethyl cellulose are considered to be most appropriate for evaluation. The TER based on the lowest LD50 for this vehicle (570 mg/kg bw) is shown in the table below.

Table 2.6.1.2-02 Toxicity Exposure Ratios for exposure of mammals to pyridaben due to consumption of contaminated grasses

appln.	Time scale	Toxicity endpoint (mg a.s./kg bw or mg a.s./kg bw/day)	Route	PEC _{FEED} or PEC _{WATER} (mg/kg ww or mg/L)	ETE (mg/kg bw/d)	TER
Citrus EU S	Acute	570	Grasses	13	18	32

The TER value in Table 2.6.1.2-02 is above the Annex VI 91/414 EEC trigger of 10 for consumption of contaminated grasses, and the risk is considered to be acceptable.

Conclusion:

The acute risk to mammals is considered to be acceptable. The long-term risk assessment due to consumption of contaminated fish is considered to be acceptable. The long-term risk assessment for the routes grasses and earthworms needs to be refined.

Risk of metabolites for mammals

A risk assessment is performed for metabolites formed at a maximum level of at least 10% TRR in plants. In plant metabolism studies, individual identified metabolites were at the most 5.1% TRR in apple fruit (25 days after treatment), 4.6% TRR in citrus fruit (7 days after the second treatment) and 1.1% TRR in tomato fruit (14 days after treatment). Hence no individual identified metabolite exceeded 10% TRR, and no assessment of plant metabolites is made.

Conclusion:

The acute and long-term risk resulting from exposure of mammals to the metabolites of pyridaben is low for both applications.

2.6.2 Effects on aquatic species**Summary of acute toxicity data**

Results of studies on the acute toxicity of pyridaben, the metabolite PB-7 and the formulations Pyridaben WP 75 and BAS 300 11 I to aquatic life are summarised in Table 2.6.2-01 to 2.6.2-04.

Table 2.6.2-01 The acute toxicity of pyridaben to aquatic life

Species	Test type	LC/EC ₅₀ (µg a.s./L)	NOEC (µg a.s./L)
Fish			
<i>Oncorhynchus mykiss</i>	Flow-through	0.73 ^(A)	0.29 ^(A)
<i>Lepomis macrochirus</i>	Flow-through	3.5 ^(A)	2.2 ^(A)
<i>Cyprinodon variegatus</i>	Flow-through	17 ^(A)	6.2 ^(A)
Invertebrates			
<i>Daphnia magna</i>	Flow-through	1.0 ^(A)	0.22 ^(A)
<i>Mysidopsis bahia</i>	Flow-through	0.67 ^(A)	0.15 ^(A)
<i>Crassostrea virginica</i>	Flow-through	8.3 ^(A)	0.20 ^(A)
Algae			
<i>Selenastrum capricornutum</i>	Static	EbC50 & ErC50 >17 ^(B)	NOEbC & NOErC 17 ^(B)
<i>Anabaena flos-aquae</i>	Static	EbC50 & ErC50 >13 ^(B)	NOEbC & NOErC 13 ^(B)
<i>Navicula pelliculosa</i>	Static	EbC50 & ErC50 >14 ^(B)	NOEbC & NOErC 14 ^(B)
<i>Skeletonema costatum</i>	Static	EbC50 & ErC50 >16 ^(B)	NOEbC & NOErC <16 ^(B)

(A) Based on mean measured concentrations

(B) Based on initial measured concentrations

Table 2.6.2-02 The acute toxicity of PB-7 to aquatic life

Species	Test type	LC/EC ₅₀ (µg a.s./L)	NOEC (µg a.s./L)
Fish			
<i>Oncorhynchus mykiss</i>	Semi-static	>8000 ^(A)	8000 ^(A)
Invertebrates			
<i>Daphnia magna</i>	Static	28 ^(A)	5 ^(A)
Algae			
<i>Selenastrum capricornutum</i>	Static	EbC50 3100 ^(B) ErC50 >16000 ^(B)	NOEbC & NOErC 540 ^(B)
Sediment-dwelling organisms			
<i>Chironomus riparius</i>	Static	140 ^(B)	<10 ^(B)

(A) Based on mean measured concentrations

(B) Based on initial measured concentrations

Table 2.6.2-03 The acute toxicity of Pyridaben 75 WP to aquatic life

Species	Test type	LC/EC ₅₀ (µg a.s./L)	NOEC (µg a.s./L)
Fish <i>Oncorhynchus mykiss</i>	Semi-static	2.2 ^(A)	0.57 ^(A)
Invertebrates <i>Daphnia magna</i>	Static	0.99 ^(B)	0.17 ^(B)
Algae <i>Selenastrum capricornutum</i>	Static	EbC50 35000 ^(B) ErC50 68000 ^(B)	NOEbC & NOErC 16000 ^(B)

(A) Based on mean measured concentrations

(B) Based on analytically confirmed nominal concentrations

Table 2.6.2-04 The acute toxicity of BAS 300 11 I to aquatic life

Species	Test type	LC/EC ₅₀ (µg a.s./L)	NOEC (µg a.s./L)
Fish <i>Lepomis macrochirus</i>	Static ^(A)	64 ^(B)	<31 ^(B)
Invertebrates <i>Mysidopsis bahia</i>	Static ^(A)	16 ^(B)	5.9 ^(B)

(A) Higher tier study outdoors

(B) Based on initial measured concentrations

Summary of chronic toxicity data

Studies on the chronic toxicity of pyridaben and BAS 300 11 I are summarised in Tables 2.6.2-05 and 2.6.2-06.

Table 2.6.2-05 The chronic toxicity of pyridaben to aquatic life

Species	Type of test	NOEC (µg a.s./L)
<i>Pimephales promelas</i>	301-day fish full life cycle test	0.28 ^(A)
<i>Daphnia magna</i>	21-day study	0.086 ^(A)
<i>Chironomus riparius</i>	28-day study	5.1 ^(B)
<i>Mysidopsis bahia</i>	35-day study	0.047 ^(A)

(A) Based on mean measured concentrations

(B) Based on initial measured concentrations

Table 2.6.2-06 The chronic toxicity of BAS 300 11 I to aquatic life.

Species	Type of test	NOEC (µg a.s./L)	NOEAEC (µg a.s./L)
Phytoplankton, zooplankton, periphyton, macroinvertebrates and fish (bluegill)	12-week microcosm study	<0.34 (2 applications at 29 days' interval) ^(A)	0.34 (2 applications at 29 days' interval) ^(A) ; EAC 0.11 ^(A)

(A) Based on nominal concentrations (analytically confirmed for initial concentrations)

Further, in microcosms containing sediment and treated with pyridaben, no treatment related mortality of fish (bluegill sunfish) was observed after 56 days at a simulated spray drift application (nominal treatment rate 1.7 µg a.s./L) followed by a simulated runoff treatment 20 hours later (nominal treatment rate 2.0 µg a.s./L).

Risk assessment (active substance)

Acute risk

The risk assessment for algae will be based on the results of the study with the formulated product. Acute risk assessment for the other organisms (fish, *Daphnia* and shrimp) will be based on the results of the studies with the active substance.

The acute TERs, based on the lowest of the available LC/EC50 values and initial PECsw values (calculated by FOCUS Step 3 for citrus, since Step 1 and 2 calculations resulted in PECsw values above water solubility and FOCUS Step 2 for tomato, since Step 1 is not considered appropriate for greenhouse treatments) for fish, *Daphnia magna*, shrimp and algae are shown in Table 2.6.2-07.

Table 2.6.2-07 Acute TERs for pyridaben for fish, *Daphnia*, shrimp and algae

Crop	Dose (kg a.s./ha)	LC/EC50 (µg as/L)				PECsw (µg as/L)	TER			
		Fish	<i>Daphnia</i>	Shrimp	Algae		Fish	<i>Daphnia</i>	Shrimp	Algae
Tomato	0.25	0.73	1.0	0.67	35000	0.0833	8.8	12	8.0	4E+05
Citrus ^(B)	0.30	0.73	1.0	0.67	35000	10.402	0.070	0.096	0.064	3365
Citrus ^(C)	0.30	0.73	1.0	0.67	35000	7.820	0.093	0.128	0.086	4476

(A) Emission rate to surface water

(B) D6 ditch scenario (FOCUS STEP 3)

(C) R4 stream scenario (FOCUS STEP 3)

The acute TERs for algae are above the Annex VI trigger of 10 for both applications and the risk is considered acceptable. The acute TERs for fish, *Daphnia magna* and *M. bahia* are all below the relevant Annex VI trigger of 100 for both applications and the risk assessment needs to be refined.

Fish and invertebrates were the most sensitive species.

A higher tier study on the acute toxicity of BAS 300 11 I (75.8% pyridaben) to Bluegill sunfish (*Lepomis macrochirus*) under outdoor conditions in tanks with sediment was submitted. The resulting 96-hour LC50 was 64 µg a.s./L, i.e. under outdoor conditions (DT50 for disappearance from water phase presumably much less than one day), bluegill sunfish was almost a factor of 20 less sensitive to pyridaben than under standard flow-through test conditions in the laboratory. In an in situ test in a microcosm study, 5 and 70% of the bluegill died after exposure to 3.4 and 34 µg a.s./L (DT50 for disappearance from water phase 0.9-1.5 days), respectively, resulting in a 96-hour LC50 of 19 µg/L. No higher tier study with rainbow trout, the most sensitive fish species (4.8 times more sensitive than bluegill sunfish in acute testing), was submitted. Trout is also likely to be less sensitive to a pulse-dose exposure to pyridaben under outdoor conditions, as compared to the flow-through or semi-static exposure in acute laboratory tests, but the risk for rainbow trout cannot be refined in the absence of higher tier studies (e.g., exposure to a realistic dosing regime under outdoor conditions).

A higher tier study on the acute toxicity of BAS 300 11 I (75.8% pyridaben) to *Mysidopsis bahia* under outdoor conditions (DT50 for disappearance from water phase much less than one day) gave a 96-h LC50 of 16 µg a.s./L. Shrimps were a factor of 24 less sensitive to pyridaben than under standard flow-through test conditions in the laboratory. Based on a LC50 value of 16 µg a.s./L, the application in tomato (TER = 192) would satisfy the Annex VI trigger of 100 for shrimp, but treatment of citrus would not (TERs 1.5-2.0).

The results of a microcosm study are evaluated at the end of this section.

Long-term risk

The long-term TERs based on the initial PEC_{sw} are shown in Table 2.6.2-08.

Table 2.6.2-08 Long-term TERs for pyridaben assuming constant exposure to the initial PECs

Crop	Dose (kg a.s./ha)	NOEC (µg as/L)				PEC _{sw} (µg a.s./L)	TER			
		Fish	<i>Daphnia</i>	<i>Chironomus</i>	<i>M. bahia</i>		Fish	<i>Daphnia</i>	<i>Chironomus</i>	<i>M. bahia</i>
Tomato	0.25	0.28	0.086	5.1	0.047	0.0833	3.4	1.0	61	0.56
Citrus ^(B)	0.30	0.28	0.086	5.1	0.047	10.402	0.027	0.008	0.49	0.0045
Citrus ^(C)	0.30	0.28	0.086	5.1	0.047	7.820	0.036	0.011	0.65	0.0060

(A) Emission rate to surface water

(B) D6 ditch scenario (FOCUS STEP 3)

(C) R4 stream scenario (FOCUS STEP 3)

The long-term TER for fish, *Daphnia*, *Chironomus* and *M. bahia* are all below the Annex VI trigger of 10, except for the long-term risk for *Chironomus* in tomato. For the other organisms and uses, the long-term risk assessment needs to be refined.

For tomato, refinement of the risk for fish and invertebrates using refinement of the PEC (additional FOCUS calculations) is not possible since only one scenario could be evaluated (glasshouses). Refinement using 21-day TWA instead of the initial PEC_{sw} values is considered not appropriate in this case, since in the microcosm study (two applications with 29 days interval, DT50 (water) 0.88-1.3 days) reductions of the populations of certain species (e.g. *Ceriodaphnia*, *Lepadella*) were observed 1-3 weeks after the initial pulse exposure to pyridaben (DT50 0.7-1.5 days), hence it cannot be excluded that effects on *Daphnia* could result from exposure occurring early on in the exposure period.

For refinement of the risk assessment for invertebrates, data from the microcosm study can be used. Following two treatments T1 and T2 (29 days' interval) of microcosms populated by phytoplankton, periphyton, zooplankton, macroinvertebrates and fish (bluegill sunfish) with BAS 300 11 I at dose levels of 0.34, 3.4 and 34 µg a.s./L, no adverse effects were observed on periphyton at nominal concentrations up to and including 34 µg a.s./L. Phytoplankton populations

(reduction of cryptophyta and increase of pyrophyta, the latter possibly an indirect effect) were significantly affected at 34 µg a.s./L. Significant treatment related negative effects on zooplankton at the community level were observed at 3.4 and 34 µg a.s./L, and significant negative effects at the population level at and above 0.34 µg a.s./L. No statistically significant effects were seen on macroinvertebrates at the community level up to a concentration of 34 µg a.s./L, but statistically significant reductions of individual taxonomic groups were observed for Hydra (at and above 3.4 µg a.s./L) and Oxyethira (at and above 0.34 µg a.s./L). Increased fish mortality was observed at 34 µg a.s./L, and mean fish length and weight were significantly higher at 34 µg a.s./L as compared to the control and lower treatments, probably due to reduced competition for food. An overall NOEC_{microcosm} of <0.34 µg a.s./L can be derived from the evaluated microcosm experiment. At the exposure level of 0.34 µg a.s./L and above, the populations of the macroinvertebrate Oxyethira were reduced at 7 days after treatment, but recovery occurred at all dose levels before study end. At the exposure level of 0.34 µg a.s./L and above, a statistically significant effect on the abundance of the rotifer *Polyarthra* was seen from day 2 after T2 through day 14 after T2, but at the next dose of 3.4 µg a.s./L full recovery of *Polyarthra* within the study was observed (but not at 34 µg a.s./L). At 3.4 µg a.s./L, adverse effects without demonstrated recovery prior to study end were recorded only for the macroinvertebrate Hydra. The NOEAEC of the evaluated microcosm study with pyridaben is therefore: 0.34 µg a.s./L. In the study summary of the monograph, the effects classes proposed by De Jong *et al.* were applied to the treatment regime of the study (two applications). The setting of the NOEAEC however was based on recovery after the second application. Therefore the NOEAEC is also applicable to the treatment regime of Nexter Pro (single application).

Taking a precautionary extrapolation factor of 3 into account, the The EAC was determined to be 0.11 µg a.s./L.

The EAC is higher than the PEC_{sw} for the application in tomato (0.0833 µg a.s./L), but lower than the PEC_{sw} for the application in citrus (7.820 µg a.s./L for the R4 stream scenario and 10.58 µg a.s./L for the D6 ditch scenario). Therefore, the risk for the application in tomato is considered to be acceptable for invertebrates, but the risk assessment for the application in citrus needs to be refined. Refinement could be performed using buffer zones. The smallest buffer zone at which the risk is acceptable is 225 m with a spray drift of 0.016%, resulting in a PEC_{sw} of 0.01087 µg a.s./L (D6 ditch scenario) or 0.0080 µg a.s./L (R4 stream scenario). TERs based on the EAC of 0.11 µg a.s./L are then above 10 (10.27 and 13.75, respectively).

The notifier is requested to submit additional data for a refined risk assessment for invertebrates and sediment-dwelling organisms for the application in citrus. This may be a FOCUS step 4 calculation for the application in citrus or any other data considered appropriate.

Two microcosm studies with fish are available. In microcosms containing sediment, no treatment related mortality of fish was observed after treatment of 1.7 + 2.0 µg a.s./L. The highest tier endpoint available for fish is the NOEC for fish of 3.4 µg a.s./L from the microcosm study containing also phytoplankton, zooplankton, periphyton and macroinvertebrates.

Only one fish species, bluegill sunfish, was included in these microcosms. This species was not the most sensitive fish species (bluegill sunfish 4.8 times less sensitive in acute testing than rainbow trout, the most sensitive species). Therefore a factor of 10 for interspecies variability should be applied to the endpoint. Furthermore, not the most sensitive fish stages were tested and only effects on mortality, length and weight and behaviour were studied, not chronic toxicity effects like reproduction. Therefore, also a factor of 3 should be applied for extrapolation from acute to chronic toxicity.

The resulting endpoint for fish is 0.11 µg a.s./L, as for invertebrates. It has already been shown that with this endpoint, triggers are not met.

The notifier argues that the relevant endpoint for fish acute risk assessment is 14.6 µg a.s./L: the lowest acute LC50 for rainbow trout (0.73 µg a.s./L) multiplied with 20 to reflect the difference in toxicity seen between lab and higher tier studies. A comparison between acute indoor and outdoor studies is made to support this. For mysid shrimp, LC50 values are 0.67 and 16 µg a.s./L for indoor and outdoor, respectively. For bluegill sunfish, these values are 3.5 and 64 µg a.s./L. For both species, the ratio between indoor and outdoor toxicity is about 20. According to the notifier, this reduction of toxicity observed under field conditions is independent of species, but reflects the dissipation process and subsequent bioavailability. Furthermore, the notifier states that the focus of the risk assessment should be at acute risk assessment and not chronic, because the ratio between acute and chronic LC50-values is <3 and because the fish life cycle study conducted with fathead minnow demonstrated limited effects over prolonged periods of exposure.

The argumentations of the notifier are not accepted. To determine whether chronic risk assessment is relevant, acute endpoints should be compared with chronic endpoints, so LC50s with NOECs. The NOEC from the FLC-study with fathead minnow is 0.28 µg a.s./L based on reduced fry growth of the parent generation, and reduced F1, egg hatchability and survival of the F1 generation. A 96-h LC50 of 2.3 µg a.s./L was determined in the FLC-study. This endpoint was not considered reliable, but is used since no acceptable study with this species is available. It is clear that for fathead minnow the ratio between acute and chronic toxicity is quite high. Therefore, chronic risk assessment should be performed. As shown above, the risk for fish is not acceptable.

Therefore, the notifier is requested to submit additional data for a refined risk assessment for fish for both applications (e.g. exposure of sensitive stages and species to a realistic dosing regime (possibly under outdoor conditions), or a FOCUS step 4 calculation for the application in citrus).

Bioaccumulation

Pyridaben has a DT90 in the whole system of a water/sediment system of ≥ 210 days. The risk for bioaccumulation should therefore be considered. Two bioconcentration studies with pyridaben under flow-through conditions were submitted. In the first study, the mean BCF for radioactivity was 346 L/kg wet weight for whole fish, but pyridaben was not detected in fish tissues. In the second study, the BCF based on parent pyridaben was <48 L/kg wet weight for whole fish (carp: 6% lipid). The Annex VI trigger factor is 100 L/kg for non-readily biodegradable substances. In birds and mammals, the risk of bioaccumulation due to the intake of contaminated fish, based on the worst-case BCF value of <48 L/kg, was considered to be low. Therefore, bioaccumulation is considered to be of no concern.

Conclusion:

The risk to algae is considered to be low for both applications. The risk for the application in tomato is considered to be acceptable for invertebrates, but the risk assessment for the application in citrus needs to be refined. The risk assessment for fish needs to be refined for both applications. The risk for bioaccumulation is considered to be low.

Risk assessment of metabolites

PB-7 was shown to be the only major ($>10\%$) metabolite in the water phase of a water/sediment system, with a maximum level of 17.2% AR in water and 14.1% AR in sediment. In an aquatic photolysis study, the DT50 for aquatic photolysis of pyridaben at 25°C (Xenon light, 425 W/m²) was 6.8 minutes, and major photodegradates were W-1 (max. 27.9% AR, DT50 <1.5 hours) and B-3 (max. 29.2% AR, photolytically stable). The risk of these metabolites must be considered. The metabolites PB-9 and P-16 were found at 8.5% and 5.2% AR, respectively, in the water phase of water-sediment systems, but since levels $>5\%$ AR were not observed at two successive samplings and levels did not increase in time, the risk of these metabolites is not considered.

Acute risk

PB-7

The worst-case TERs for this metabolite are summarised in the table below.

Table 2.6.2-09 Acute TERs for PB-7

Crop	LC/EC50 (µg/L)				PECsw (µg/L)	TER			
	Fish	<i>Daphnia</i>	Algae	<i>Chironomus</i>		Fish	<i>Daphnia</i>	Algae	<i>Chironomus</i>
Tomato	>8000	28	3100	150	0.0153	$>5E+05$	1830	$2E+05$	9804
Citrus	>8000	28	3100	150	3.0982	>2582	9.0	1001	48

For the application in tomato, the acute TERs of PB-7 for fish, *Daphnia*, algae and *Chironomus* are all far above the relevant Annex VI triggers (100, 100, 10 and 100, respectively). Hence the acute risk should be low for this application. For the application in citrus, a risk is considered to be present for *Daphnia* and *Chironomus* and the risk assessment needs to be refined.

Exposure of aquatic organisms to this metabolite during the microcosm study is likely to have occurred. The EAC was however lower than the PEC_{sw} for pyridaben for the application in citrus, and the risk for this application was concluded to need further refinement. Therefore, the risk for PB-7 for the application in citrus awaits fulfilment of the requirements for pyridaben.

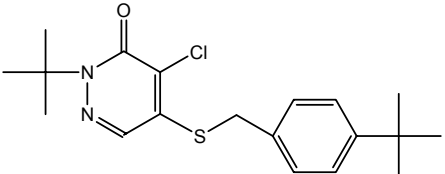
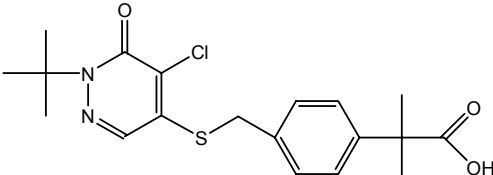
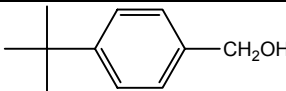
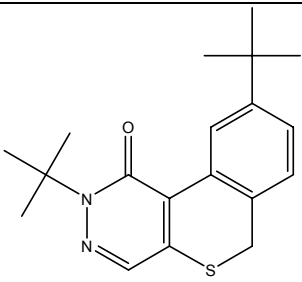
W-1 and B-3

No studies on acute toxicity with W-1 and B-3 are available. The photolytic DT50 of pyridaben was 6.8 minutes at a light intensity of 425 W/m². This light intensity is comparable to the light intensity measured on earth in Europe (450 W/m², midsummer, 40°N). Therefore, the toxicity of these photolytic metabolites should be covered by the microcosm study, and the risk of both metabolites is considered to be low for algae and invertebrates for the application in tomato, for which the PEC is covered by the EAC of 0.11 µg a.s./L. As the EAC does not cover the PEC for the application in citrus, a separate assessment is given below.

The relative toxicities of these metabolites cannot be predicted by structural considerations alone. Therefore, the toxicities of these metabolites were estimated by RMS using EPA EPI Suite software (Ecosar). The results are summarised in the table below.

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be gained on the basis of this document.

Table 2.6.2-10 Structures of pyridaben and it's metabolites, and experimentally determined and estimated toxicity endpoints

Structure	Name (max. % AR in water)	Endpoint	Test (μg a.s./L) ^(B)	Estimate (μg a.s./L) ^(C)
	Pyridaben	Fish 96 hr LC50 <i>Daphnia</i> 48 hr EC50 Algae 72 hr EC50	0.73 1.0 35000	40-43 17-738 152-697
	PB-7 (17.2%)	Fish 96 hr LC50 <i>Daphnia</i> 48 hr EC50 Algae 72 hr EC50	>8000 28 3100	2376-4937 16712-20618 10924-29175
	B-3 (29.2%)	Fish 96 hr LC50 <i>Daphnia</i> 48 hr EC50 Algae 72 hr EC50		5152-13935 15989 10582
	W-1 (27.9%)	Fish 96 hr LC50 <i>Daphnia</i> 48 hr EC50 Algae 72 hr EC50		1177-1698 2131 1520

(A) Maximum level in whole system (water/sediment)

(B) Endpoint from submitted studies

(C) Estimated by RMS using EPA EPI Suite software (Ecosar)

As can be read from Table 2.6.2-10, estimated endpoints for pyridaben are lower than those for all metabolites. Furthermore, the differences in sensitivity for pyridaben between algae, fish and daphnia were the same for estimated and experimentally determined endpoints. The estimated endpoints for PB-7 for fish and algae (but not for *Daphnia*) are in reasonable agreement with the experimentally determined endpoints. Since the estimated lower toxicity of PB-7 is confirmed by experimental data, the estimated toxicity values for the other two metabolites B-3 and W-1 may be used in a qualitative risk assessment. The maximum levels of the aqueous photodegradates W-1 and B-3 were respectively 27.9% and 29.2% AR.

Both metabolites are estimated to be far less toxic to algae than parent pyridaben, and of comparable or slightly higher toxicity to algae than PB-7. Considering the large safety margins calculated for the risk of parent pyridaben and PB-7 to algae (TER values 3E+03 and 1001, respectively), and the PECsw values for W-1 and B-3 (4.2286 and 2.2128 $\mu\text{g/L}$), which are lower

than that of pyridaben (7.820-10.420 µg/L) and slightly higher or lower than that of PB-7 (3.0982 µg/L), the risk of W-1 and B-3 to algae should be low for the treatment of citrus.

B-3 is estimated to be far less toxic to fish than parent pyridaben, and of comparable toxicity to fish as PB-7. Considering the large safety margin calculated for the risk of PB-7 to fish (TER >2582) and the PEC_{sw} value for B-3 (2.2128 µg/L), which is lower than that of PB-7 (3.0982 µg/L), the acute risk of B-3 to fish should be low for the treatment of citrus (and hence for that of tomato). B-3 is estimated to be far less toxic to daphnia than parent pyridaben, but of slightly higher toxicity to daphnia than PB-7. Since the TER of PB-7 to *Daphnia* for treatment of citrus was 9.0, the estimates indicate a possible risk of B-3 to *Daphnia* for treatment of citrus, even though the PEC_{sw} value for B-3 (2.2128 µg/L) is slightly lower than that of PB-7 (3.0982 µg/L).

W-1 is estimated to be far less toxic to fish than parent pyridaben, but of higher toxicity (by a factor of about 5) to fish than PB-7. Although the safety margin calculated for the risk of PB-7 to fish was large for treatment of citrus (TER >2582, i.e. a factor of 26 above the trigger of 100), there is insufficient ground to conclude with certainty that the risk of W-1 for treatment of citrus to fish will also be low, in spite of its short-lived existence (DT₅₀ <1.5 hours). The reasons are that there may be a large uncertainty in the toxicity estimate, and that there is very close structural similarity between W-1 and parent pyridaben, suggesting that they may be of comparable toxicity. The risk of W-1 to fish for treatment of tomato should be low however, considering the large safety margin for PB-7 (TER>5E+05) and the only slightly higher PEC_{sw} value for W-1 (4.2286 µg/L) as compared to that of PB-7 (3.0982 µg/L). W-1 is estimated to be less toxic (factor of about 3) to daphnia than parent pyridaben, but of higher toxicity to daphnia (factor of about 10) than PB-7. Since the TER of pyridaben and PB-7 to *Daphnia* for treatment of citrus was 0.095 and 9.0, respectively, the estimates indicate a possible risk of W-1 to *Daphnia* for treatment of citrus.

The risk of B-3 and W-1 to *Daphnia*, and that of W-1 to fish should be addressed. This may be done by submitting acute toxicity studies with these metabolites, but fulfillment of the data requirements for parent pyridaben (e.g., restriction on label, or studies in which exposure to metabolites is also addressed) may also address the issues for metabolites.

Long-term risk

PB-7

PB-7 is acutely not more toxic than parent pyridaben. Therefore, chronic testing with water organisms is not required for this metabolite. PB-7 was a major metabolite in sediment, with a maximum level of 14% AR after 120 days in a water/sediment study, and testing with sediment-dwelling organisms is required. Toxicity of this metabolite should be covered by the microcosm study. Therefore, the risk for this metabolite is considered to be low for the application in tomato, but the risk assessment for the application in citrus awaits fulfillment of the data requirement for parent pyridaben. Alternatively, a test with *Chironomus riparius* may be submitted.

W-1 and B-3

Since the acute toxicity of W-1 and B-3 is expected to be lower than that of pyridaben (Table 2.6.2-10), testing with these metabolites is not necessary.

Conclusion long-term risk assessment of metabolites

Chronic exposure of aquatic organisms to metabolites is considered to be of no concern for both applications. The chronic risk of PB-7 to sediment-dwelling organisms needs to be considered after fulfillment of the data requirements of parent pyridaben (e.g., restrictions on label, studies in which exposure to metabolites is also addressed, or a chronic study with *Chironomus riparius*).

Bioaccumulation

No experimentally determined BCF values in fish are available for PB-7, B-3 and W-1. LogPow values were estimated by the RMS using EPA EPI Suite software and Pallas 3.0 software. The BCF for fish can be estimated according to the formula $\log BCF = 0.85 \cdot \log Pow - 0.7$ (USES 2.0). The estimated logPow values and estimated BCF values are presented in the table below.

Table 2.6.2-11 LogPow and BCF-values for metabolites of pyridaben

Metabolite	EPA EPI Suite		Pallas	
	LogPow ^(A)	BCF (L/kg)	logPow ^(B)	BCF (L/kg)
PB-7	3.86	381	3.67	263
B-3	2.99	69	2.94	63
W-1	4.29	884	4.96	3281

(A) Estimated by RMS using EPA EPI Suite software

(B) Estimated by RMS using Pallas 3.0 software

The estimated BCF value of B-3 is below the Annex VI trigger of 100, while those of PB-7 and W-1 are above 100. W-1 was a photolytic degradate of pyridaben that was formed at it's maximum level of 16% AR within 0.5 hours. W-1 has a DT50 of <1.5 hours, and therefore, it's risk for bioaccumulation should be low.

In order to further assess the risk for bioaccumulation, the concentration in fish for PB-7 is estimated by multiplying the mean BCF with the concentration of the metabolite in water. Since presence of PB-7 in rats and hens was not unequivocally confirmed, and PB-7 was only found at 0.7% AR in faeces and 3.8% TRR in livers of goats dosed with parent pyridaben, the toxicity of this metabolite cannot be assumed to be covered by parent pyridaben, and the concentration of PB-7 in fish cannot be compared to the NOEC for the parent. Therefore, the maximum NOEC value that would indicate a risk due to bioaccumulation for birds and mammals is calculated from the concentration in fish, according to $NOEC < 5 \cdot ETE$, where $ETE = PEC_{feed} \cdot DF / BW$. The results for the application in citrus are shown in the table below.

Table 2.6.2-12 Mean BCF-values and maximum NOEC that leads to risk for metabolites of pyridaben

Application in citrus				Birds			Mammals		
Metabolite	Mean BCF	PEC _{sw} (mg/L)	PEC _{fish} (mg/kg)	NOEC pyridaben (mg/kg)	NOEC metabolite for TER<5	factor more toxic	NOEC pyridaben (mg/kg)	NOEC metabolite for TER<5	factor more toxic
PB-7	322	3.1E-03	1.0	10	1.03	9.7	1.87	0.65	2.9

The results in Table 2.6.2-12 show that a risk due to bioaccumulation of PB-7 exists if the long-term toxicity of PB-7 is at least a factor of 2.9 higher than that of parent pyridaben. PB-7 was less toxic than parent pyridaben to fish, daphnia and algae by a factor of at least 28. In rat, PB-7 was also less toxic by a factor of 2.8-4.8 than parent pyridaben (LD₅₀ for pyridaben in carboxymethylcellulose 570-1100 mg/kg bw; LD₅₀ for PB-7 tested in carboxymethylcellulose 2728-3086 mg/kg bw). The available toxicity data for PB-7 do not indicate that it has a higher toxicity than pyridaben. Furthermore, the BCF calculated for PB-7 is based on the assumption that PB-7 is not further degraded in fish, which is not likely. Therefore, the risk due to bioaccumulation for PB-7 should be low.

Conclusion:

The acute risk of PB-7 to fish, *Daphnia*, algae and *Chironomus* should be low for the application in tomato. For the application in citrus, an acute risk of PB-7 is considered to be present for *Daphnia* and *Chironomus* and the risk assessment needs to be refined. The acute risk of W-1 and B-3 to algae should be low for the treatment of citrus. The acute risk of B-3 to fish should be low for the treatment of citrus (and hence for that of tomato). The risk of B-3 and W-1 to *Daphnia*, and that of W-1 to fish should be addressed.

Chronic exposure of aquatic organisms to metabolites is considered to be of no concern for both applications. The chronic risk of PB-7 to sediment-dwelling organisms needs to be considered after fulfilment of the data requirements of parent pyridaben.

2.6.3 Effects on bees and other arthropod species

2.6.3.1 Bees

The calculation of hazard quotients (HQs) is based on the acute oral and contact LD₅₀ values, determined for the active substance (0.535 and 0.024 µg a.s./bee, respectively). The hazard quotients for the treatment of tomato and citrus are presented in Table 2.6.3.1-01.

Table 2.6.3.1-01 Hazard quotients for honey bees using laboratory toxicity studies on Pyridaben 10EC formulation

Crop	dose (g a.s./ha)	oral toxicity		contact toxicity		Annex VI trigger
		LD50 (µg a.s./bee)	HQ	LD50 (µg a.s./bee)	HQ	
Tomato EU N & S	250	0.535	467	0.024	10417	50
Citrus EU S	300	0.535	561	0.024	12500	50

The HQs are all above the trigger of 50 specified in Annex VI of 91/414 EC, and higher tier testing is required to evaluate the risk to bees.

Higher tier risk assessment

An aged residue study, four tunnel tests, one field test and one bee brood study with formulated products were submitted. The residue study showed that survival, which was significantly reduced at 0.56 kg a.s./ha, increased with aging of residues, but was still significantly reduced after 24 hours of aging. The field test was not acceptable due to insufficient information on test procedures and important guideline deviations. A bee brood study with Pyridaben 20 WP showed no adverse effects on brood of honey bees fed sucrose solution with 100 mg/L pyridaben. Repellency was observed however during the study and it was uncertain that the study result could be extrapolated to other pyridaben based formulations, since it is unclear whether the repellency is due to pyridaben or to co-formulants. Furthermore, the NOEC (100) mg a.s./L is lower than the concentration in the spray liquid of Nexter Pro (400 mg a.s./L) and thus does not cover the uses applied for anyway. Therefore, the risk assessment will be based on the tunnel tests with BAS 9078 0 I, BAS 9078 4 I and Nexter, all containing 20% pyridaben. In three tunnel tests, where bee survival and behaviour were assessed, increased bee mortality during the first day and reduced foraging behaviour were observed at dose rates of 1.2 kg a.s./ha (four times the maximum recommended rate for pyridaben). In the fourth tunnel test, which included assessments of brood-comb development, increased bee mortality on the day of treatment and adverse effects on bee brood development were observed at a dose rate of 0.15 kg a.s./ha. This dose rate is lower than the proposed doses in citrus in Southern Europe (1 x 0.30 kg a.s./ha) and tomato in Northern and Southern Europe (1 x 0.25 kg a.s./ha). Therefore, a risk to bees is considered to be present.

The notifier is therefore requested to submit additional data for an adequate risk assessment (e.g. an acceptable field study). Alternatively, the notifier may include a phrase on the label stating that application is only allowed in greenhouses equipped with insect mesh and in which bees are not used as pollinators, whilst treatment in the field should not be made on flowering crops, and spraying of flowering weeds must be avoided.

Risk of metabolites

A risk assessment is performed for metabolites formed at a maximum level of at least 10% TRR in plants. In plant metabolism studies, individual identified metabolites were at the most 5.1% TRR in apple fruit (25 days after treatment), 4.6% TRR in citrus fruit (7 days after the second treatment) and 1.1% TRR in tomato fruit (14 days after treatment). Hence no individual identified metabolite exceeded 10% TRR, and no assessment of plant metabolites is made.

2.6.3.2 Other arthropod species

For the proposed use in tomato (single application rate of 0.25 kg a.s./ha) and citrus (single application rate of 0.30 kg a.s./ha), it is assumed for in-field environments that 100% of the dose will be deposited. For the use in citrus, it is assumed for off-field environments that 15.73% (90th percentile, 1 application, 3 m buffer zone; late stage) of the dose will be deposited in the non-target area. For the application in tomato (greenhouse), off-field exposure is not applicable. Table 2.6.3.2-01 below summarises the results of standard laboratory testing with non-target arthropod species.

Table 2.6.3.2-01 Summary of effects of Pyridaben 75WP on non-target arthropod species during laboratory testing on inert substrate

Species	Life stage	Test type, substrate and duration	Actual dose tested (g a.s./ha)	Endpoint	Effect (%) at respective dose in test and LR50 and ER50 values
<i>Typhlodromus pyri</i>	Protonymphs	Laboratory, glass, 14 days	0.05; 0.10; 0.20; 0.40; 0.80; 1.6 (fresh residues)	Mortality Reduction of reproduction	4.3; 4.3; -4.4 ^(A) ; 13; 84; 99 LR50 (g a.s./ha): 0.59 37; 26; 33; 36; n.a. ^(B) ; n.a. ^(B) ER50 (g a.s./ha): >0.40
<i>Aphidius rhopalosiphi</i>	Adults	Laboratory, glass, 2 days	0.05; 0.10; 0.20; 0.40; 0.80; 1.6 (fresh residues)	Mortality Reduction of reproduction	0; 5; 60; 73; 88; 100 LR50 (g a.s./ha): 0.24 35; -17 ^(A) ; 48; 48; n.a. ^(B) ; n.a. ^(B) ER50 (g a.s./ha): 0.20

(A) Note: negative effect %, hence no adverse effect

(B) n.a. = not applicable (insufficient survivors from initial phase to assess reproduction)

According to Annex II of 91/414, data must be submitted on two sensitive species and two species that are relevant to the intended use. Annex II refers to the SETAC Guidance Document on Regulatory Testing Procedures for Pesticides with Non-target Arthropods (Barrett *et al.*, 1994) as a source of guidance for testing. Since several limitations have been identified in this Guidance

document it is proposed that the risk to non-target arthropods both in and off-field should be addressed according to the recommendations of ESCORT 2.

A Tier I assessment is performed using the data from the initial laboratory studies on inert substrate with *T. pyri* and *A. rhopalosiphi*. For this standard risk assessment, the following scenarios are used to describe the exposure in-field and off-field. For both the key input is the nominal field application rate supplemented by various factors:

in-field exposure= Application rate * MAF

off-field exposure= Application rate * MAF * (drift factor / vegetation distribution factor)

As the proposed worst-case use of the Pyridaben 75 WP formulation involves 1 application at the highest dose (citrus in Southern Europe, 300 g a.s./ha), the multiple application factor (MAF) for the maximum dose is 1. The drift factor for off-field exposure was based on the 90th percentile drift data and corrected by a "vegetation distribution factor" of 10%.

The LR50 for *Typhlodromus pyri* and *Aphidius rhopalosiphi* on fresh dried residue on glass was determined as 0.59 and 0.24 g a.s./ha, respectively. These values were used for hazard quotient (HQ) calculation for in-field and off-field exposure: in-field HQ= in-field exposure/LR50 and off-field exposure= (off-field exposure/LR50)*uncertainty factor. An uncertainty (safety) factor of 10 was included in the off-field Hazard Quotient calculations to account for uncertainty with the extrapolation from *Typhlodromus pyri* and *Aphidius rhopalosiphi* as indicator species, to all off-field non-target arthropods. The risk is considered acceptable if HQ <2. The table below summarises the results.

Table 2.6.3.2-02 Risk to *Typhlodromus pyri* and *Aphidius rhopalosiphi* as a result of in-field (0 m) and off-field (3 m) exposure of the proposed Pyridaben 75 WP formulation in tomato in Northern and Southern Europe and citrus in Southern Europe (Hazard Quotient Approach; vegetation distribution factor off-field of 10), based on LR50 and ER50 values from inert substrate

Crop / species	dose g as/ha	distance (m)	% drift	Exposure (g a.s./ha)	LR50 (g a.s./ha)	HQ	trigger value
<i>Typhlodromus pyri</i>							
Tomato EU N & S	250	0	-	250	0.59	424	2
Citrus EU S	300	0	-	300	0.59	508	2
		3	15.73	4.7	0.59	80	2
<i>Aphidius rhopalosiphi</i>							
Tomato EU N & S	250	0	-	250	0.24	1042	2
Citrus EU S	300	0	-	300	0.24	1250	2
		3	15.73	4.7	0.24	197	2

The HQs for in-field exposure are above the trigger of 2 for both applications. The HQs for off-field exposure are above 2 for the application in citrus. The off-field HQ values for *T. pyri* and *A. rhopalosiphi* are only below the trigger value of 2 if buffer zones of at least 40 and 75 m are used,

respectively (*T. pyri*, 40 m and *A. rhopalosiphi*, 75 m: HQ=1.6 and 1.4, respectively). Such large buffer zones are considered unrealistic, and therefore, a risk is considered to be present.

Since the in-field HQ values for both indicator species are above the trigger of 2 for both applications, and the off-field HQ values are above 2 for the application in citrus, higher tier data are required for these two species, as well as for two additional species. Data were submitted from extended laboratory studies with *T. pyri*, *A. rhopalosiphi*, *C. carnea* and *E. formosa*, and from greenhouse studies with *E. formosa* and *O. niger*. In addition, data were submitted from field studies with *N. californicus* & *P. ulmi* and *T. pyri*, as well as from field studies with field populations of arthropods in a citrus orchard in Spain and an apple orchard in France. The extended and greenhouse study with *E. formosa* and the field studies with *N. californicus* & *P. ulmi* and *T. pyri* were not acceptable due to the lack of information on study procedures and test substance identification, and the greenhouse studies with *E. formosa* and *O. niger* were concluded to be useful only as supplementary information.

Therefore, the data from the extended laboratory studies with *T. pyri*, *A. rhopalosiphi* and *C. carnea*, and the field studies with field populations of arthropods in a citrus orchard in Spain and an apple orchard in France are used for a higher tier risk assessment. Results from these studies are summarised in the table below.

Table 2.6.3.2-03 Summary of effects of Pyridaben 75WP on non-target arthropod species during extended laboratory testing

Species	Life stage	Test type, substrate and duration	Actual dose tested (g a.s./ha)	Endpoint	Effect (%) at respective dose in test and LR50 and ER50 values
<i>Typhlodromus pyri</i>	Protonymphs	Extended laboratory, fresh residues on apple leaf discs, 14 days	47; 200; 300	Mortality Reduction of reproduction	80; 96; 93 LR50 (g a.s./ha): <47 n.a. ^(A) ; n.a. ^(A) ; n.a. ^(A) ER50 (g a.s./ha): <47
		Extended laboratory, 7-day aged residues on apple leaf discs, 14 days	47; 200; 300	Mortality Reduction of reproduction	86; 96; 99 LR50 (g a.s./ha): <47 n.a. ^(A) ; n.a. ^(A) ; n.a. ^(A) ER50 (g a.s./ha): <47
		Extended laboratory, 14-day aged residues on apple leaf discs, 14 days	47; 200; 300	Mortality Reduction of reproduction	3.2; 56; 80 LR50 (g a.s./ha): 155 2; n.a. ^(A) ; n.a. ^(A) ER50 (g a.s./ha): >47
		Extended laboratory, 21-day aged residues on apple leaf discs, 14 days	47; 200; 300	Mortality Reduction of reproduction	1.1; 7.7; 46 LR50 (g a.s./ha): 300 1; 11; 17 ER50 (g a.s./ha): >300
		Extended laboratory, 28-day aged residues on apple leaf discs, 14 days	300	Mortality Reduction of reproduction	32 LR50 (g a.s./ha): >300 22 ER50 (g a.s./ha): >300
<i>Aphidius rhopalosiphii</i>	Adults	Extended laboratory, fresh residues on apple leaves, 2 days	47; 200; 300	Mortality Reduction of reproduction	92; 100; 100 LR50 (g a.s./ha): <47 n.a. ^(A) ; n.a. ^(A) ; n.a. ^(A) ER50 (g a.s./ha): <47
		Extended laboratory, 7-day aged residues on apple leaves, 2 days	47; 200; 300	Mortality Reduction of reproduction	70; 100; 100 LR50 (g a.s./ha): <47 n.a. ^(A) ; n.a. ^(A) ; n.a. ^(A) ER50 (g a.s./ha): <47
		Extended laboratory, 14-day aged residues on apple leaves, 2 days	47; 200; 300	Mortality Reduction of reproduction	43; 98; 100 LR50 (g a.s./ha): 56 71; n.a. ^(A) ; n.a. ^(A) ER50 (g a.s./ha): <47

Species	Life stage	Test type, substrate and duration	Actual dose tested (g a.s./ha)	Endpoint	Effect (%) at respective dose in test and LR50 and ER50 values
		Extended laboratory, 21-day aged residues on apple leaves, 2 days	47; 200; 300	Mortality	7.9; 68; 92
				Reduction of reproduction	LR50 (g a.s./ha): 123 0; 91; n.a. ^(A) ER50 (g a.s./ha): 104
		Extended laboratory, 28-day aged residues on apple leaves, 2 days	47; 200; 300	Mortality	13; 36; 82
				Reduction of reproduction	LR50 (g a.s./ha): 172 52; 78; n.a. ^(A) ER50 (g a.s./ha): 42
		Extended laboratory, 35-day aged residues on apple leaves, 2 days	47; 200; 300	Mortality	0; 35; 74
				Reduction of reproduction	LR50 (g a.s./ha): 208 8; 12; 70 ER50 (g a.s./ha): 261
		Extended laboratory, 42-day aged residues on apple leaves, 2 days	200; 300	Mortality	18; 60
				Reduction of reproduction	LR50 (g a.s./ha): 272 77; 32 ER50 (g a.s./ha): >300
		Extended laboratory, 49-day aged residues on apple leaves, 2 days	200; 300	Mortality	42; 2.8
				Reduction of reproduction	LR50 (g a.s./ha): >300 -144 ^(B) ; -103 ^(B) ER50 (g a.s./ha): >300
<i>Chrysoperla carnea</i>	2 nd instar larvae	Extended laboratory, fresh residues on field treated apple leaves, until adult emergence	53; 247; 308	Reduction of reproduction	6; -32 ^(B) ; -35 ^(B) ER50 (g a.s./ha): >308
		Extended laboratory, 15-day aged residues on field-treated apple leaves, until adult emergence	53; 247; 308	Reduction of reproduction	42; -4 ^(B) ; 36 ER50 (g a.s./ha): >308

(A) n.a. = not applicable (insufficient survivors from initial phase to assess reproduction)

(B) Note: negative effect %, hence no adverse effect

For the higher tier risk assessment, scenarios are similar to those used in the Tier I assessment, with the following exceptions: the application rate is multiplied by a factor of 0.5 for the application in citrus (3-dimensional crop situation); for off-field, the vegetation distribution factor is not included since in the studies, whole plants were treated; for off-field, the uncertainty factor is 5. The risk is considered acceptable if the effects at the calculated in- and off-field rates are <50% (ESCORT 2). The in-field rate calculated for the application in tomato is 250 g a.s./ha. The in- and off (3 m)-field

exposure rate for citrus, calculated according to the methods in ESCORT 2 (i.e. for off-field with omission of the vegetation distribution factor of 10), are 150 and 118 g a.s./ha, respectively.

Table 2.6.3.2-04 gives an overview of the LR50 and ER50 values obtained in the extended laboratory studies with *T. pyri*, *A. rhopalosiphi* and *C. carnea*.

Table 2.6.3.2-04 LR50 and ER50 values for *Typhlodromus pyri*, *Aphidius rhopalosiphi* and *C. carnea* as a result of exposure to the proposed Pyridaben 75 WP formulation in extended laboratory studies with fresh and aged residues

Ageing of residues (days)	<i>T. pyri</i>		<i>A. rhopalosiphi</i>		<i>C. carnea</i>	
	LR50 (g a.s./ha)	ER50 (g a.s./ha)	LR50 (g a.s./ha)	ER50 (g a.s./ha)	LR50 (g a.s./ha)	ER50 (g a.s./ha)
0	<47	<47	<47	<47	>308	>308
7	<47	<47	<47	<47		
14	155	>47	56	<47	>308 ^(A)	>308 ^(A)
21	300	>300	123	104		
28	>300	>300	172	42		
35			208	261		
42			272	>300		
49			>300	>300		

(A) 15-day aged residues instead of 14-day aged residues

Effects >50% on survival and reproduction were observed in the extended laboratory studies with *T. pyri* and *A. rhopalosiphi* when exposed to fresh residues at a dose rate of 47 g a.s./ha, which is below the calculated worst-case in- and off-field rates of 250 and 118 g a.s./ha, respectively. With ageing of the residues, the effects decreased. After 21 and 42 days, respectively, the LR50 and ER50 values for *T. pyri* and *A. rhopalosiphi* were above the in-field dose rates in tomato and citrus of 250 and 150 g a.s./ha. After 21 and 35 days, respectively, the LR50 and ER50 values for *T. pyri* and *A. rhopalosiphi* are above the off-field rate of 118 g a.s./ha as well. Effects <50% were observed in the extended laboratory study with *C. carnea* at 308 g a.s./ha, which is above the highest in- and off-field rates of 250 and 118 g a.s./ha, respectively. This data for the two indicator species and for one additional species is sufficient to demonstrate that there is potential of recovery of affected in-field populations of non-target arthropods after treatment of tomato. However, for off-field populations, aged-residue studies are not sufficient to address recovery, because for off-field it is less sure that recolonisation is possible. Off-field areas will often be narrow, and especially for the less mobile surface dwellers recolonisation will be difficult. Therefore, for off-field actual recovery must be shown, not just potential for recovery as done with an aged-residue test. Also, since the Tier I assessment for citrus showed that there was an in-field and an off-field risk, testing of two additional species under extended laboratory conditions is required.

During field studies with field populations of arthropods in a citrus orchard in Spain and an apple orchard in France, no significant effects were observed at the highest tested dose rates of 47 and 39 g a.s./ha, respectively. These dose rates are lower than the in- and off-field rates calculated for citrus. However, bigger buffer zones can be taken into account. The off-field rate for citrus using a buffer zone of 10 m (drift value 3.60%) is 27 g a.s./ha. Therefore, these field studies address the potential for recovery of affected arthropod populations for the application in citrus, provided that a buffer zone of 10 m is used.

It should be noted that in this approach, the calculation of the off-field rate includes the correction factor of 5. This factor, meant to cover inter-species variability in sensitivity of off-field non-target arthropod species, could be lowered considering the fact that in the field tests many different species were tested. However, ESCORT 2 does not specify how much it should be lowered, and no consensus has been reached so far about this. RMS is of the opinion that some kind of safety factor should still be applied, for the following reasons: 1) In the field studies, surface dwellers were not included in the sampling, while surface dwellers make up an important part of the off-field fauna. 2) The species sensitivity distributions of in-field and off-field fauna might differ considerably. Since citrus needs regular use of PPPs, it is to be expected that the in-field species present in a citrus crop have been selected on their high capacity for recovery after disturbance (from e.g. PPPs), which means that they have a higher recovery capacity than the off-field species. Also, the off-field community is more diverse than the in-field community.

In the case of pyridaben, using a correction factor of 2 would lead to an off-field drift rate of 47 g a.s./ha and thus to an acceptable risk without the use of buffer zones. However, due to the uncertainties and lack of knowledge surrounding the issue of correction factors, RMS does not propose any lowered correction factor.

Overall conclusion

The in-field risk to non-target arthropods for the application in tomato is acceptable. For this greenhouse application, off-field exposure is not applicable. Tier I assessment indicates an in- and an off-field risk to non-target arthropods of treatment of citrus, but extended laboratory studies with two standard species and one additional species (*C. carnea*) suggest that there is potential of recovery of affected in- and off-field populations of non-target arthropods. Two field studies confirm this. However, the test dose rates in these field studies are lower than the in- and off-field rates for citrus. Therefore, the in- and off-field risk in citrus is also acceptable, provided that a buffer zone of 10 m is used.

Risk of metabolites

A risk assessment is performed for metabolites formed at a maximum level of at least 10% TRR in plants. In plant metabolism studies, individual identified metabolites were at the most 5.1% TRR in apple fruit (25 days after treatment), 4.6% TRR in citrus fruit (7 days after the second treatment)

and 1.1% TRR in tomato fruit (14 days after treatment). Hence no individual identified metabolite exceeded 10% TRR, and no assessment of plant metabolites is made.

2.6.4 Effects on earthworms and other soil macro-organisms

2.6.4.1 Effects on earthworms

Active substance

Risk assessment will be based on the corrected LC50 value ($LC50_{corr}$) for the active substance, since pyridaben has a logPow of >6.37. A chronic toxicity/reproductive study with Pyridaben 75 WP was submitted (NOEC 0.29 mg a.s./kg soil). The NOEC was determined in a soil with 5% organic matter and therefore, the NOEC need not be corrected.

The acute TER is presented in Table 2.6.4.1-01.

Table 2.6.4.1-01 Acute risk of pyridaben to earthworms

appln.	dose (kg a.s./ha)	$LC50_{corr}$ (mg a.s./kg)	PECs (mg a.s./kg)	Acute TER	Annex VI trigger 91/414 EEC
Tomato EU N & S	0.25	19	0.077	247	10
Citrus EU S	0.30	19	0.139	137	10

The TER values in Table 2.6.4.1-01 are far above the Annex VI 91/414 EEC trigger of 10. Hence the acute risk of pyridaben to earthworms is considered to be acceptable.

The long-term TER is presented in Table 2.6.4.1-02.

Table 2.6.4.1-02 Chronic risk of pyridaben to earthworms

appln.	dose (kg a.s./ha)	NOEC (mg a.s./kg)	PECs (mg a.s./kg)	Chronic TER	Annex VI trigger 91/414 EEC
Tomato EU N & S	0.25	0.29	0.077	3.8	5
Citrus EU S	0.30	0.29	0.139	2.1	5

The TER values in Table 2.6.4.1-02 are below the Annex VI 91/414 EEC trigger of 5, and a long-term risk of pyridaben to earthworms cannot be excluded. According to the Guidance Document on Terrestrial Risk Assessment, a field study is required when the TER is below 5. A field study was submitted, but this study was considered to be insufficiently reliable to be taken to the list of endpoints because of the lack of pre-test worm counts, the lack of verification of the applied dose by chemical analysis of the soil, and the lack of a positive control. The notifier is therefore requested to provide additional data for further risk assessment for earthworms (e.g. an acceptable earthworm field study).

A new earthworm field study is currently in progress.

Risk assessment of metabolites

Pyridaben was the main component of the residue in soil. The maximum level of the main degradation products PB-4 and PB-7 in any of the investigated soils was 7.6% and 8.5% AR, respectively. Since levels of >5% AR were found on 2 or more successive samplings, the risk of these metabolites should be considered. In a photodegradation study in soil, PB-22 was found at a maximum level of 13% AR, and the risk of this metabolite must be considered. Given the low levels of individual metabolites in soil, and the fact that the acute TERs for the parent compound (137-247) were clearly on the safe side, the acute risk of the soil metabolites of pyridaben is considered to be low.

Chronic toxicity/reproductive studies on metabolites of pyridaben were not submitted. Chronic studies are not required when the field DT90 is <100 days (Sanco/10329/2002). Field or lab DT90 values are not available for metabolites. In cases where the DT90 value is >365 days, a sublethal study with earthworms is required. The Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC (Working Document Sanco/10329/2002 rev 2 final, 17 October 2002) does not provide guidance for the case where the DT90 is between 100 and 365 days and the number of applications is less than three. In the update of the HTB (Dutch Manual for Authorisation of Pesticides), the Netherlands will propose to require chronic/reproductive data in cases where the 100 days <field DT90 <365 days, if the TERa >10 and ≤100. Considering the large safety margin calculated for the acute risk of pyridaben (TERa = 137-247), and the much lower levels of metabolites compared to those of the parent compound, it is considered unlikely that the TERa values for the soil metabolites will be ≤100. Therefore, chronic/reproductive data are not required when the DT90 values of the soil metabolites are between 100 and 365 days, but only when the DT90 exceeds 1 year.

PB-7 is a minor (<10%) soil metabolite, which was less toxic than parent pyridaben to fish, daphnia and algae by a factor of at least 28. In rat, PB-7 was also less toxic by a factor of 2.5-5.4 than parent pyridaben (LD50 for pyridaben in carboxymethylcellulose 570-1100 mg/kg bw; LD50 for PB-7 tested in carboxymethylcellulose 2728-3086 mg/kg bw). Although direct extrapolation from these species to earthworms is not justified, the available toxicity data for PB-7 do not indicate that it has a higher toxicity than pyridaben. The likelihood that PB-7 is more toxic to earthworms than parent pyridaben is considered to be low, and if the long-term risk for pyridaben is found to be acceptable, the risk for PB-7 need not be further tested. The assessment for PB-7 therefore awaits fulfilment of the data requirement for long-term risk for pyridaben.

Furthermore, the notifier is requested to submit additional data for the chronic risk assessment of the soil metabolites PB-4 and PB-22 of pyridaben (e.g. DT90 values, or a field study with pyridaben in earthworms, where the risk of metabolites will be addressed).

2.6.4.2 Effects on other soil macro-organisms

The Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC (Sanco 10329/2002, rev 2 final) states that testing is required if the field DT90 values in soil are >100 days. Since the (maximum) field DT90 value for pyridaben is 424 days, hence >1 year, a litter-bag test is required. A litter-bag study was submitted. The litter-bag study showed no inhibitory effects on soil litter degradation at a total measured dose of 0.11 mg a.s./kg soil. This is only slightly lower than the worst case soil plateau maximum PEC (0.139 mg a.s./kg, section B.8.3), and much higher than the average plateau PEC (0.061 mg a.s./kg, section B.8.3).

Also, a collembola test was submitted, in which the NOEC was 3.28 mg a.s./kg soil (2.33% oc). The resulting TER values, based on PEC_{soil} values of 0.077 and 0.139 mg a.s./kg for the application in tomato and citrus, respectively, are 43 and 24, and hence above the trigger value of 5.

Considering these results, the risk of pyridaben for soil non-target macro-organisms is considered to be acceptable.

Metabolites

The need for testing of metabolites depends on the field DT90. DT90 values are however not available for any of the soil metabolites of pyridaben. A litter-bag study was submitted, in which soil litter degradation was studied during 365 days. Since all soil metabolites of pyridaben were formed within 5 months in aerobic degradation studies, these metabolites are considered to have been covered by the litter-bag test. Therefore, the risk of the metabolites for soil non-target macro-organisms is considered to be acceptable.

2.6.5 Effects on soil micro-organisms

Studies on the toxicity of pyridaben on soil microbial respiration and nitrification were submitted in two soils. The study on effects on respiration was found to be acceptable for both soils (sandy loam, 21% particles >200 µm, 1.4% organic carbon; and loamy sand, 70% particles >200 µm, 0.6% organic carbon), while the study on nitrification was found to be acceptable for one soil only (loamy sand, 70% particles >200 µm, 0.6% organic carbon). Only the loamy sand soil fully meets the requirement of a sensitive soil laid down in the SETAC document on Procedures for assessing the environmental fate and ecotoxicity of pesticides (1995). The data submitted are considered to be sufficient.

The NOEC for effects on nitrification of a loamy sand soil and on respiration of the sandy loam soil and the loamy sand soil treated with pyridaben was 8.0 mg a.s./kg soil.

The worst case soil plateau maximum PEC of pyridaben (0.139 mg a.s./kg) is a factor of 58 below the highest test concentration of pyridaben without lasting effects on soil microbial activity (8.0 mg a.s./kg). Furthermore, the litterbag study showed no inhibitory effects on soil litter degradation at a total measured dose of 0.11 mg a.s./kg soil. This is only slightly lower than the worst case soil plateau maximum PEC, and much higher than the average plateau PEC (0.061 mg a.s./kg). Therefore, the risk of pyridaben for soil microflora is considered to be acceptable.

Risk assessment of metabolites

A risk assessment should be performed for soil metabolites formed at a maximum level of at least 10% AR (major metabolites), for metabolites formed at two successive samplings at a level of at least 5% AR, and for metabolites for which an increasing trend of formation is observed in soil degradation studies.

In laboratory incubated soil, the maximum level of the main degradation products PB-4 and PB-7 in any of the incubations was 7.6% and 8.5% AR, respectively. Since levels of >5% AR were found at two successive samplings, the risk of these metabolites should be considered. In a photodegradation study in soil, PB-22 was found at a maximum level of 13% AR, and the risk of this metabolite must be considered.

PB-4 and PB-7

No separate studies on the effects of metabolites of pyridaben to soil micro-organisms have been submitted. The maximum percentage of formation of these metabolites in any laboratory incubated soil was reached after 150 and 60 days, respectively. The levels of these two metabolites were however low (mean maximum level for all tested soils 4.6% and 4.3% AR, respectively). Moreover, these metabolites appeared already early during incubation, and the mean maximum level within 29-30 days (2.4% and 3.0% AR respectively) represented 60% and 70% of the mean maximum level observed in soil. Exposure of soil micro-organisms to these metabolites is therefore assumed to have occurred at a sufficient level to conclude that their effects have been covered by studies with parent pyridaben to soil micro-organisms, which were conducted at a 58x overdose compared to the PEC_{soil}. Consequently, the risk of these metabolites to soil micro-organisms is considered to be low.

PB-22

Only in one of five tested soils PB-22 could be identified separately, and in this soil the maximum level was 1.2% AR (PB-22, within 7 days). In a study on four other soils, PB-22 and PB-14 could not be separated by HPLC, and maximum levels of the cluster of up to 6.2% AR (mean for four soils 3.9% AR) were reached late during the study (after 120-151 days). Since in three of five tested soils the levels of the cluster of PB-14 and PB-22 within 29-30 days were very low (0%, 0.1% and 0.6% AR), whilst the occurrence of relatively high levels of the cluster after 4-5 months (6.2% AR) was also observed, it is uncertain that the effects of PB-22 were covered by the studies on effects of parent pyridaben to soil microflora (respiration and nitrification). However, PB-22 can be assumed to have been formed in the litterbag study. Therefore, the risk of PB-22 to soil micro-organisms is acceptable.

2.6.6 Effects on other non-target organisms (flora and fauna)

In a seedling emergence test and a vegetative vigor test, effects on seedling emergence, survival, plant height and biomass were $\leq 23\%$ for all ten species tested at a dose rate of 0.56 kg a.s./ha. *In vitro* seed germination was not affected by more than 7% in any of the species tested at a concentration of 1.5 mg a.s./L.

A Tier I assessment is performed according to the recommendations in the Working Document (Sanco/10329/2002). A preliminary risk assessment is based on the available data of initial laboratory screening. The risk is considered acceptable if less than 50% effect is observed at the maximum application rate (300 g a.s./ha for the application in citrus). Effects were $\leq 23\%$, hence well below 50%, in all ten plant species at a dose of 560 g a.s./ha, a dose 1.9 times higher than the maximum application rate. Therefore, the risk for plants is considered to be acceptable.

2.6.7 Effects on biological methods of sewage treatment

Given the nature of the proposed uses, it is unlikely that pyridaben will reach sewage treatment works. In any case, this compound caused no inhibition of the bacterial respiratory rate in the study submitted (EC50 >100 mg a.s./L). Consequently the risk to sewage treatment processes is acceptable.

APPENDIX 1

PYRIDABEN

PART 1: Standard terms and abbreviations

PART 2: Organisations and publications

PART 3: Preparation (formulation) types and codes

Part 1 Standard terms and abbreviations

A	ampere
ACh	acetylcholine
AChE	acetylcholinesterase
ADI	acceptable daily intake
ADP	adenosine diphosphate
AE	acid equivalent
AFID	alkali flame-ionisation detector or detection
A/G	albumin/globulin ratio
ai	active ingredient
ALD ₅₀	approximate median lethal dose, 50%
ALT	alanine aminotransferase (SGPT)
AOEL	acceptable operator exposure level
AMD	automatic multiple development
ANOVA	analysis of variance
AP	alkaline phosphatase
approx	approximate
ARC	anticipated residue contribution
ARfD	acute reference dose
as	active substance
AST	aspartate aminotransferase (SGOT)
ASV	air saturation value
ATP	adenosine triphosphate
BCF	bioconcentration factor
bfa	body fluid assay
BOD	biological oxygen demand
bp	boiling point
BSAF	biota-sediment accumulation factor
BSE	bovine spongiform encephalopathy
BSP	bromosulfophthalein
Bt	bacillus thuringiensis
Bti	bacillus thuringiensis israelensis
Btk	bacillus thuringiensis kurstaki
Btt	bacillus thuringiensis tenebrionis
BUN	blood urea nitrogen
bw	body weight
c	centi- ($\times 10^{-2}$)
°C	degree Celsius (centigrade)
CA	controlled atmosphere
CAD	computer aided design
CADDY	computer aided dossier and data supply (an electronic dossier interchange and archiving format)
cd	candela
CDA	controlled drop(let) application
cDNA	complementary DNA
CEC	cation exchange capacity
cf	confer, compare to
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CL	confidence limits
cm	centimetre
CNS	central nervous system
COD	chemical oxygen demand

CPK	creatinine phosphatase
cv	coefficient of variation
Cv	ceiling value
CXL	Codex Maximum Residue Limit (Codex MRL)
d	day
DES	diethylstilboestrol
DFR	dislodgeable foliar residue
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic Acid
dna	designated national authority
DO	dissolved oxygen
DOC	dissolved organic carbon
dpi	days post inoculation
DRES	dietary risk evaluation system
DT ₅₀	period required for 50 percent dissipation (define method of estimation)
DT ₉₀	period required for 90 percent dissipation (define method of estimation)
dw	dry weight
DWQG	drinking water quality guidelines
ε	decadic molar extinction coefficient
EC ₅₀	median effective concentration
ECD	electron capture detector
ECU	European currency unit
ED ₅₀	median effective dose
EDI	estimated daily intake
ELISA	enzyme linked immunosorbent assay
e-mail	electronic mail
EMDI	estimated maximum daily intake
EPMA	electron probe micro analysis
ERC	environmentally relevant concentration
ERL	extraneous residue limit
F	field
F ₀	parental generation
F ₁	filial generation, first
F ₂	filial generation, second
FIA	fluorescence immunoassay
FID	flame ionisation detector
FOB	functional observation battery
fp	freezing point
FPD	flame photometric detector
FPLC	fast protein liquid chromatography
g	gram
G	glasshouse
GAP	good agricultural practice
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GEP	good experimental practice
GFP	good field practice
GGT	gamma glutamyl transferase
GI	gastro-intestinal
GIT	gastro-intestinal tract

GL	guideline level
GLC	gas liquid chromatography
GLP	good laboratory practice
GM	geometric mean
GMO	genetically modified organism
GMM	genetically modified micro-organism
GPC	gel-permeation chromatography
GPPP	good plant protection practice
GPS	global positioning system
GSH	glutathion
GV	granulosevirus
h	hour(s)
H	Henry's Law constant (calculated as a unitless value) (see also K)
ha	hectare
Hb	haemoglobin
HCG	human chorionic gonadotropin
Hct	haematocrit
HDT	highest dose tested
hL	hectolitre
HEED	high-energy electron diffraction
HID	helium ionisation detector
HPAEC	high performance anion exchange chromatography
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography - mass spectrometry
HPPLC	high pressure planar liquid chromatography
HPTLC	high performance thin layer chromatography
HRGC	high resolution gas chromatography
H _s	Shannon-Weaver index
Ht	haematocrit
I	indoor
I ₅₀	inhibitory dose, 50%
IC ₅₀	median immobilisation concentration or median inhibitory concentration
ICM	integrated crop management
ID	ionisation detector
IEDI	international estimated daily intake
IGR	insect growth regulator
im	intramuscular
inh	inhalation
ip	intraperitoneal
IPM	integrated pest management
IR	infrared
ISBN	international standard book number
ISSN	international standard serial number
iv	intravenous
IVF	in vitro fertilisation
k	kilo
K	Kelvin or Henry's Law constant (in atmospheres per cubic meter per mole, see also H)
K _{ads}	adsorption constant
K _{des}	apparent desorption coefficient
K _{oc}	organic carbon adsorption coefficient
K _{om}	organic matter adsorption coefficient
kg	kilogram
L	litre
LAN	local area network

LASER	light amplification by stimulated emission of radiation
LBC	loosely bound capacity
LC	liquid chromatography
LC-MS	liquid chromatography- mass spectrometry
LC ₅₀	lethal concentration, median
LCA	life cycle analysis
LC _{Lo}	lethal concentration low
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD ₅₀	lethal dose, median; dosis letalis media
LD _{Lo}	lethal dose low
LDH	lactate dehydrogenase
LOAEC	lowest observable adverse effect concentration
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOEC	lowest observable effect concentration
LOEL	lowest observable effect level
LOQ	limit of quantification (determination)
LPLC	low pressure liquid chromatography
LSC	liquid scintillation counting or counter
LSD	least squared denominator multiple range test
LSS	liquid scintillation spectrometry
LT	lethal threshold
m	metre
M	molar
µm	micrometer (micron)
MC	moisture content
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MDL	method detection limit
MFO	mixed function oxidase
µg	microgram
mg	milligram
MHC	moisture holding capacity
min	minute(s)
mL	millilitre
MLT	median lethal time
MLD	minimum lethal dose
mm	millimetre
mo	month(s)
mol	Mole(s)
MOS	margin of safety
mp	melting point
MRE	maximum residue expected
MRL	maximum residue level or limit
mRNA	messenger ribonucleic acid
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
n	normal (defining isomeric configuration) or number of observations
NAEL	no adverse effect level
nd	not detected
NEDI	national estimated daily intake
NEL	no effect level
NERL	no effect residue level
ng	nanogram

nm	nanometer
NMR	nuclear magnetic resonance
no	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NOIS	notice of intent to suspend
NPD	nitrogen-phosphorus detector or detection
NPV	nuclear polyhedrosis virus
NR	not reported
NTE	neurotoxic target esterase
OC	organic carbon content
OCR	optical character recognition
ODP	ozone-depleting potential
ODS	ozone-depleting substances
OM	organic matter content
op	organophosphorous pesticide
Pa	Pascal
PAD	pulsed amperometric detection
2-PAM	2-pralidoxime
pc	paper chromatography
PC	personal computer
PCV	haematocrit (packed corpuscular volume)
PEC	predicted environmental concentration
PEC _A	predicted environmental concentration in air
PEC _S	predicted environmental concentration in soil
PEC _{SW}	predicted environmental concentration in surface water
PEC _{GW}	predicted environmental concentration in ground water
PED	plasma-emissions-detector
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIC	prior informed consent
pic	phage inhibitory capacity
PIXE	proton induced X-ray emission
pKa	negative logarithm (to the base 10) of the dissociation constant)
PNEC	predicted no effect concentration
po	by mouth
P _{OW}	partition coefficient between n-octanol and water
POP	persistent organic pollutants
ppb	parts per billion (10 ⁻⁹)
PPE	personal protective equipment
ppm	parts per million (10 ⁻⁶)
ppp	plant protection product
ppq	parts per quadrillion (10 ⁻²⁴)
ppt	parts per trillion (10 ⁻¹²)
PSP	phenolsulfophthalein
PrT	prothrombin time
PRL	practical residue limit
PT	prothrombin time
PTDI	provisional tolerable daily intake
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship

r	correlation coefficient
r ²	coefficient of determination
RBC	red blood cell
REI	restricted entry interval
Rf	retardation factor
RfD	reference dose
RH	relative humidity
RL ₅₀	median residual lifetime
RNA	ribonucleic acid
RP	reversed phase
rpm	rotations per minute
rRNA	ribosomal ribonucleic acid
RRT	relative retention time
RSD	relative standard deviation
s	second
SAC	strong adsorption capacity
SAP	serum alkaline phosphatase
SAR	structure/activity relationship
SBLC	shallow bed liquid chromatography
sc	subcutaneous
sce	sister chromatid exchange
SD	standard deviation
se	standard error
SEM	standard error of the mean
SEP	standard evaluation procedure
SF	safety factor
SFC	supercritical fluid chromatography
SFE	supercritical fluid extraction
SIMS	secondary ion mass spectroscopy
SOP	standard operating procedures
sp	species (only after a generic name)
SPE	solid phase extraction
SPF	specific pathogen free
spp	subspecies
sq	square
SSD	sulphur specific detector
SSMS	spark source mass spectrometry
STEL	short-term exposure limit
STMR	supervised trials median residue
t	tonne (metric ton)
t _½	half-life (define method of estimation)
T ₃	tri-iodothyroxine
T ₄	thyroxine
TADI	temporary acceptable daily intake
TBC	tightly bound capacity
TCD	thermal conductivity detector
TC _{Lo}	toxic concentration, low
TID	thermionic detector, alkali flame detector
TD _{Lo}	toxic dose low
TDR	time domain reflectrometry
TER	toxicity exposure ration
TER _i	toxicity exposure ration for initial exposure
TER _{st}	toxicity exposure ration following repeated exposure
TER _{LT}	toxicity exposure ration following chronic exposure
tert	tertiary (in a chemical name)

TEP	typical end-use product
TGGE	temperature gradient gel electrophoresis
TIFF	tag image file format
TLC	thin layer chromatography
TIm	median tolerance limit
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TMRC	theoretical maximum residue contribution
TMRL	temporary maximum residue limit
TOC	total organic carbon
Tremcard	Transport emergency card
tRNA	transfer ribonucleic acid
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UF	uncertainty factor (safety factor)
ULV	ultra low volume
UV	ultraviolet
v/v	volume ratio (volume per volume)
WBC	white blood cell
wk	week
wt	weight
w/v	weight per volume
ww	wet weight
w/w	weight per weight
XRFA	X-ray fluorescence analysis
yr	year
<	less than
=	less than or equal to
>	greater than
=	greater than or equal to

Part 2 Organisations and Publications

ACPA	American Crop Protection Association
ASTM	American Society for Testing and Materials
BA	Biological Abstracts (Philadelphia)
BART	Beneficial Arthropod Registration Testing Group
CA	Chemical Abstracts
CAB	Centre for Agriculture and Biosciences International
CAC	Codex Alimentarius Commission
CAS	Chemical Abstracts Service
CCFAC	Codex Committee on Food Additives and Contaminants
CCGP	Codex Committee on General Principles
CCPR	Codex Committee on Pesticide Residues
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Food
CE	Council of Europe
CIPAC	Collaborative International Pesticides Analytical Council Ltd
COREPER	Comite des Representants Permanents
EC	European Commission
ECB	European Chemical Bureau
ECCA	European Crop Care Association
ECDIN	Environmental Chemicals Data and Information Network of the European Communities
ECDIS	European Environmental Chemicals Data and Information System
ECE	Economic Commission for Europe
ECETOC	European Chemical Industry Ecology and Toxicology Centre
ECLO	Emergency Centre for Locust Operations
ECMWF	European Centre for Medium Range Weather Forecasting
ECPA	European Crop Protection Association
EDEXIM	European Database on Export and Import of Dangerous Chemicals
EHC (number)	Environmental Health Criteria (number)
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMIC	Environmental Mutagens Information Centre
EPA	Environmental Protection Agency
EPO	European Patent Office
EPPO	European and Mediterranean Plant Protection Organization
ESCORT	European Standard Characteristics of Beneficials Regulatory Testing
EU	European Union
EUPHIDS	European Pesticide Hazard Information and Decision Support System
EUROPOEM	European Predictive Operator Exposure Model
FAO	Food and Agriculture Organization of the UN
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FRAC	Fungicide Resistance Action Committee
GATT	General Agreement on Tariffs and Trade
GAW	Global Atmosphere Watch
GIFAP	Groupement International des Associations Nationales de Fabricants de Produits Agrochimiques (now known as GCPF)
GCOS	Global Climate Observing System
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GEDD	Global Environmental Data Directory
GEMS	Global Environmental Monitoring System
GIEWS	Global Information and Early Warning System for Food and Agriculture
GRIN	Germplasm Resources Information Network

HRAC	Herbicide Resistance Action Committee
IARC	International Agency for Research on Cancer
IATS	International Academy of Toxicological Science
IBT	Industrial Bio-Test Laboratories
ICBB	International Commission of Bee Botany
ICBP	International Council for Bird Preservation
ICES	International Council for the Exploration of the Seas
ICPBR	International Commission for Plant-Bee Relationships
ILO	International Labour Organization
IMO	International Maritime Organisation
IOBC	International Organisation for Biological Control of Noxious Animals and Plants
IPCS	International Programme on Chemical Safety
IRAC	Insecticide Resistance Action Committee
IRC	International Rice Commission
ISCO	International Soil Conservation Organization
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JECFA	FAO/WHO Joint Expert Committee on Food Additives
JFCMP	Joint FAO/WHO Food and Animal Feed Contamination Monitoring Programme
JMP	Joint Meeting on Pesticides (WHO/FAO)
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
NATO	North Atlantic Treaty Organisation
NAFTA	North American Free Trade Agreement
NCI	National Cancer Institute (USA)
NCTR	National Centre for Toxicological Research (USA)
NGO	non-governmental organisation
NTP	National Toxicology Programme (USA)
OECD	Organisation for Economic Co-operation and Development
OLIS	On-line Information Service of OECD
PAN	Pesticide Action Network
RNN	Re-registration Notification Network
RTECS	Registry of Toxic Effects of Chemical Substances (USA)
SCPH	Standing Committee on Plant Health
SETAC	Society of Environmental Toxicology and Chemistry
SI	Système International d'Unités
SITC	Standard International Trade Classification
TOXLINE	Toxicology Information On-line
UN	United Nations
UNEP	United Nations Environment Programme
WCDP	World Climate Data Programme
WCP	World Climate Programme
WCRP	World Climate Research Programme
WFP	World Food Programme
WHO	World Health Organization
WTO	World Trade Organization
WWF	World Wildlife Fund

Part 3 Preparation (formulation) types and codes

Code	Description	Definition
AB	Grain bait	Special forms of bait.
AE	Aerosol dispenser	A container-held preparation which is dispersed generally by a propellant as fine droplets/particles upon actuation of a valve.
AL	Other liquids to be applied undiluted	Self defining.
BB	Block blits	Special forms of bait.
BR	Brique	Solid block designed for controlled release of active ingredient into water.
CB	Bait concentrate	A solid or liquid intended for dilution before use as a bait.
CG	Encapsulated granule	A granule with a protective or release controlling coating.
CS	Capsule suspension	A stable suspension of capsules in a fluid normally intended for dilution with water before use.
DC	Dispersible concentrate	A liquid homogeneous preparation to be applied as a solid dispersion after dilution in water.
DP	Dustable powder	A free-flowing powder suitable for dusting.
DS	Powder for dry seed treatment	A powder for application in the dry state directly to seed.
EC	Emulsifiable concentrate	A liquid, homogenous preparation to be applied as an emulsion after dilution in water.
ED	Electrochargeable liquid	Special liquid preparation for electrostatic (electrodynamic)spraying
EO	Emulsion. water in oil	A fluid, heterogeneous preparation consisting of a dispersion of fine globules of pesticide in water in a continuous organic liquid phase.
ES	Emulsion for seed treatment	A stable emulsion for application to the seed either directly or after dilution.
EW	Emulsion. Oil in water	A fluid, heterogeneous preparation consisting of a dispersion of fine globules of pesticide in an organic liquid in a continuous water phase.
FD	Smoke tin	Special form of smoke generator.
FG	Fine granule	A granule in the particle size range from 300 to 2500 µm.
FK	Smoke candle	A smoke generator in the form of a candle.
FP	Smoke cartridge	Special form of smoke generator.
FR	Smoke rodlet	Special form of smoke generator.
FS	Flowable concentrate for seed treatment	A stable suspension for application to the seed either directly or seed treatment after dilution.
FT	Smoke tablet	Special form of smoke generator.
FU	Smoke generator	A combustible preparation generally solid, which upon ignition releases the active substances in the form of a smoke.

Code	Description	Definition
FW	Smoke pellet	Special form of smoke generator.
GA	Gas	A gas packed in pressure bottle or pressure tank.
GB	Granular bait	Special forms of bait.
GE	Gas generating product	A preparation which generates a gas by chemical reaction.
GG	Macrogranule	A granule in the particle size range from 2000 to 6000 μ m.
GP	Flo-dust	Very fine dustable powder for pneumatic application in glasshouses.
GR	Hot fogging concentrate	A free-flowing solid preparation of a defined granule size range ready for use.
GS	Cold fogging concentrate	Very viscous preparation based on oil or fat.
HN	Hot fogging concentrate	A preparation suitable for application by fogging equipment either directly or after dilution.
KN	Cold fogging concentrate	A preparation suitable for application by cold fogging equipment, either directly or after dilution.
LA	Lacquer	A solvent based film-forming preparation.
LS	Solution for seed treatment	A solution for application to the seed either directly or after dilution.
MG	Microgranule	A granule in the particle size range from 100 to 600 μ m.
OF	Oil miscible flowable (=oil active substances in a miscible suspension)	A stable suspension of concentrate fluid intended for dilution in an organic liquid before use.
OL	Oil miscible liquid	A liquid, homogenous preparation to be applied as a homogenous liquid after dilution in an organic liquid.
OP	Oil dispersible powder	A powder preparation to be applied as a suspension after dispersion in an organic liquid.
PA	Paste	A water based film forming preparation.
PB	Plate bait	Special forms of bait.
PC	Gel or paste concentrate	A solid preparation to be applied as a gel or a paste after dilution with water.
PR	Plant rodlet	A small rodlet, usually a few centimetres in length and a few millimetres in diameter containing active substance.
PS	Seed coated with a pesticide	Self defining.
RB	Bait (ready for use)	A preparation designed to attract and be eaten by the target species.
SB	Scrap bait	Special forms of bait.
SC	Suspension (= flowable concentrate)	A stable suspension of active substance(s) in a fluid intended for dilution with water before use
SE	Suspo-emulsion	A fluid, heterogeneous preparation consisting of a stable dispersion of active substance(s) in the form of solid particles.

Code	Description	Definition
SG	Water soluble granules	A preparation consisting of granules to be applied as a true solution of active substance after dissolution in water but many contain insoluble inert ingredients.
SL	Soluble concentrate	A liquid homogenous preparation to be applied as a true solution of active substance after dissolution in water but many contain insoluble inert ingredients.
SO	Spreading oil	A preparation designed to form a surface layer on application to water.
SP	Water soluble powder	A powder preparation to be applied as a true solution of the active substance after solution in water but which may contain insoluble inert ingredients.
SS	Water soluble powder for seed treatment	A powder to be dissolved in water before application to the seed.
SU	Ultra low volume (ULV) suspension	A suspension ready for use through ULV equipment.
TB	Tablet	Solid preparation in the form of small flat plates for dissolution in water.
TP	tracking powder	A rodenticidal contact preparation in powder form.
UL	Ultra low volume (ULV) liquid	A homogenous liquid ready for use through ULV equipment.
VP	Vapour releasing product	A preparation containing one or more volatile ingredients, the vapours of which are released into the air. Evaporation rate normally is controlled by using suitable preparations and/or dispensers.
WG	Water dispersible	A preparation granule consisting of granules to be applied after disintegration and dispersion in water.
WP	Wettable powder	A powder preparation to be applied as a suspension after dispersion in water.
WS	Water dispersible powder for slurry seed treatment	A powder to be dispersed at high concentration in water before application as a slurry to the seed.
XX	Others	

APPENDIX 2

PYRIDABEN

SPECIFIC TERMS AND ABBREVIATIONS

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Specific terms and abbreviations

a	absolute organ weight
AAP	Algal Assay Procedure medium
aerob	aerobic test conditions
a-GT	alpha-glutamyl-transferase
ALAT	alanine aminotransferase
ALP	alkaline phosphatase
amu	atomic mass units
anaer	anaerobic test conditions
AR	applied radioactivity
ASAT	aspartate aminotransferase
ASTM	American Society for Testing and Materials
B	bacteria
biodeg	biodegradation
Chr. ab.	chromosome aberrations
CMC	carboxymethylcellulose
CoE	Council of Europe
crit.	criterion
d	decreased, but not statistically significantly
dc	statistically significantly decreased
DFI	Daily Food Intake
DMF	dimethylformamide
DO	Dissolved Oxygen
dr	dose-related
DWI	Daily Water Intake
E	total effect of mortality and fecundity/parasitic capacity, used in arthropod toxicity tests
E. coli	<i>Escherichia coli</i>
equal	used when the values given by the notifier are expressed in mg/kg bw/day.
equivalent	used when values given by the notifier are only expressed in mg/kg food, not in mg/kg bw/day, as species-dependent factor is used to translate these data to mg/kg bw/day.
ETE	Estimated Theoretical Exposure
GCP	good clinical practice
GIDH	glutamic-acid dehydrogenase

GOT	glutamic-oxalacetic transaminase
GPT	glutamic-pyruvic transaminase
HDL	high density lipoproteins
HPRT	hypoxanthine- guanine phosphoribosyl transferase
i	increased, but not statistically significantly
ic	statistically significantly increased
MC	moisture content in soil (v/v)
Mc	mammalian cells
MWHC	maximum water holding capacity (soils)
n/a	not applicable
n.d.	not detected
n.r.	not reported
ns	not significant
o.m.	organic matter
PEC	Predicted Environmental Concentration
PEG	polyethylene glycol
pF	moisture tension (soil) in [log cm _{water column}]
PIEC	Predicted Initial Environmental Concentration
pointmut.	pointmutations
r	relative organ weight
r.a.	radioactivity
res.	result
Ri	Reliability Index, referring to the intrinsic reliability of a test with respect to the quality of the study
S. typh.	<i>Salmonella typhimurium</i>
SPE	Solid Phase Extraction
Sub.	Substance
T	temperature
TWA	time weighted average
TWAE	time weighted average environmental concentration

wat/sed	water/sediment systeem
w/w	weight per weight
-	negative
+	positive
-act.	without activation
+act.	with activation
%v/v	the percentage expressed by volume
%w/w	the percentage expressed by weight

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APPENDIX 3

PYRIDABEN

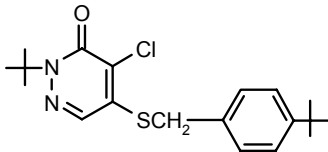
LIST OF END-POINTS

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Chapter 2.1 Identity, Physical and Chemical Properties, Details of Uses, Further Information**Identity, Physical and Chemical Properties, Details of Uses, Further Information**

Active substance (ISO Common Name)	Pyridaben
Function (e.g. fungicide)	Insecticide, acaricide
Rapporteur Member State	The Netherlands

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyrididin-3(2H)-one
Chemical name (CA)	4-chloro-2-(1,1-dimethylethyl)-5-[[[4-(1,1-dimethylethyl)phenyl]methyl]thio]-3(2H)-pyridazinone
CIPAC No	583
CAS No	96489-71-3
EEC No (EINECS or ELINCS)	405-700-3
FAO Specification (including year of publication)	Not available
Minimum purity of the active substance as manufactured (g/kg)	980 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None
Molecular formula	C ₁₉ H ₂₅ ClN ₂ OS
Molecular mass	364.9
Structural formula	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity)	109.4 to 110.6°C (100.0%)
Boiling point (state purity)	thermal decomposition was observed before boiling occurred (100.0%).
Temperature of decomposition (state purity)	thermal degradation and elimination of volatile decomposition products from 200 to 400°C (100.0%)

Appearance (state purity)	Pure material: white crystalline solid (100.0%)
	Technical material: white crystalline powder (98.3%)
Vapour pressure (state temperature, state purity)	$<1 \times 10^{-5}$ Pa at 52.7°C (98%)
Henry's law constant	$<3 \times 10^{-1}$ Pa.m ³ .mol ⁻¹ at 25°C (calculated from a vapour pressure determined at 53°C and a water solubility ²⁾ determined at 24°C) <i>Open</i> until final water solubility study is performed.
Solubility in water (state temperature, state purity and pH)	0.012 mg/L ¹⁾ in distilled water at 24°C (99.6%) Effect of pH was not investigated since there is no dissociation in water in the environmentally relevant pH-range A new study is required.
Solubility in organic solvents (state temperature, state purity)	Solubility at 20°C in g/L (98.3%) xylene: 345 dichloromethane: >1000 acetone: 333 ethyl acetate: 305 Solubility at 25°C in g/L (98.3%) acetonitrile: 95.2 1-octanol: 71.1 methanol: 49.4 n-hexane: 14.1
Surface tension (state concentration and temperature, state purity)	not applicable since the water solubility is below 1 mg/L (i.e. 0.012 mg/L) <i>Open</i> until final water solubility study is performed.
Partition co-efficient (state temperature, pH and purity)	Log P _{o/w} >6.37 at 23°C (99.6%) Effect of pH was not investigated since there is no dissociation in water in the environmentally relevant pH-range
Dissociation constant (state purity)	Pyridaben does not dissociate

UV/VIS absorption (max.) incl. ϵ
(state purity, pH)

neutral, acidic and basic solutions in methanol at 24.2°C (100.0%)		
Medium / Concentration (mol/L)/pH	Absorbance maxima (nm)	Molar absorption coefficient (L/(molxcm))
Neutral / 5.654×10^{-5}	296.5	11746
	236.2	21102
	223.4	23221
Acidic / 5.654×10^{-5} (pH 0.85)	296.9	11785
	236.3	21142
	223.3	23327
Basic / 5.654×10^{-5} (pH 13.19)	296.6	11724
	236.3	21015
	223.2	23037

Flammability (state purity)

not flammable (purity not specified, data required)
no auto-ignition up to 475°C (98.3%)

Explosive properties (state purity)

explosive (sensitive to friction) (purity not specified, **data required**)

Oxidising properties (state purity)

not oxidizing (99.2%)

Classification and proposed labelling (Annex IIA, point 10)

Active substance

RMS/peer review proposal

E, R2

Summary of representative uses evaluated (pyridaben)*

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 application s (min)	kg as/ha min max	water l/ha min max		
Citrus	Southern MS	Nexter Pro, Sanmite 75 WP	F	Mites Whitefly	WP	750 g/l	Tractor mounted / trailed broadcast air assisted sprayer	At infestation on No later than BBCH 83	1	na	0.005 – 0.04	750 – 6000	14	
Tomato	Northern and Southern MS	Nexter Pro, Sanmite 75 WP	G	Mites Whitefly	WP	750 g/l	Various hydraulic sprayers	At infestation on No later than BBCH 89	1	na	0.005 – 0.04	625 – 5000	3	

* For uses where the column "Remarks" is marked in grey further consideration is necessary.

Uses should be crossed out when the notifier no longer supports this use(s).

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)

(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)

(c) e.g. biting and sucking insects, soil born insects, foliar fungi, weeds

(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) GC/PC Codes - GIFA/ 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 plant- type of equipment used must be indicated

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypry). In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiazincarb-isopropyl).

(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) Indicate the minimum and maximum number of application possible under practical conditions of use

(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha)

(m) PHI - minimum pre-harvest interval

Chapter 2.2 Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	Dissolution in acetonitrile containing internal standard (1-phenyl-dodecanone) followed by HPLC-UV
Impurities in technical as (analytical technique)	Dissolution in acetonitrile followed by HPLC-UV
Plant protection product (analytical technique)	Dissolution in acetonitrile containing internal standard (1-phenyl-dodecanone) followed by HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	Pyridaben
Food of animal origin	No residue definition required
Soil	pyridaben, PB-22
Water surface	pyridaben, PB-7, W-1, B-3
drinking/ground	pyridaben, PB-4, PB-7, PB-22
Air	pyridaben, PB-22, PB-7, B-3
Blood and tissues	pyridaben

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	GC-ECD method D9309 (pyridaben): 0.05 mg/kg (orange fruit & orange process products) GC-ECD method D9312 (pyridaben): 0.05 mg/kg (tomato) Confirmatory LC-MS/MS method (pyridaben) Level: 0.5 mg/kg (orange fruit & orange process products)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	No methods required because no residue definition for animal products is proposed.
Soil (analytical technique and LOQ)	LC-MS/MS (no method number specified): 0.01 mg/kg (pyridaben)
Water (analytical technique and LOQ)	LC-MS/MS (no method number specified): 0.005 µg/L (pyridaben) matrix: tap, ground and surface water
Air (analytical technique and LOQ)	HPLC-UV (no method number specified): 1.0 µg/m³

Body fluids and tissues (analytical technique and LOQ)

Tissues: GC-ECD (D9405) LOQ 0.05 mg/kg (fat, kidney, muscle, liver)

Blood: HPLC-MS/MS (no method number specified):
LOQ 0.05 mg/l

(OPEN)

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Chapter 2.3 Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	20 % (based on urinary (11-19%) excretion within 168 h)
Distribution ‡	Highest residues in liver, kidneys, uterus, ovary and lymph nodes at 2 h.
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	Extensive within 72 h: mainly via faeces (67-84%), 4-24% via urine, <0.07% via expired air (168 h)
Metabolism in animals ‡	Metabolised; many metabolites were identified, but the identification of only a few was confirmed.
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound
Toxicologically relevant compounds ‡ (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD ₅₀ oral ‡	≥ 161 mg/kg bw	R25
Rat LD ₅₀ dermal ‡	> 2000 mg/kg bw	
Rat LC ₅₀ inhalation ‡	> 0.62 mg/L air /4h (whole body)	R23
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant	
Skin sensitisation (M&K)‡	Non-sensitising	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Reduced body weight gain or/and body weight	
Relevant oral NOAEL ‡	3-month, dog, 1.0 mg/kg bw/day	
	1-year, dog, 1.0 mg/kg bw/day	
Relevant dermal NOAEL ‡	4-week, rat, 100 mg/kg bw/day	
Relevant inhalation NOAEL ‡	4-week, rat, 3.0mg/m ³ (0.84 mg/kg bw/day)	

Genotoxicity ‡ (Annex IIA, point 5.4)

Pyridaben is unlikely to be genotoxic <i>in vivo</i>	
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Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Reduced body weight gain or/and body weight	
Relevant NOAEL ‡	78-week, mouse, 0.81 mg/kg bw/day	
	2-year, rat, 1.1 mg/kg bw/day	

Carcinogenicity ‡

Pyridaben is unlikely to pose a carcinogenic risk to humans	
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Reproductive toxicity (Annex IIA, point 5.6)**Reproduction toxicity**

Reproduction target / critical effect ‡

No reproductive effects.

Relevant parental NOAEL ‡

1.87 mg/kg bw/day (decreased body weight gain and food consumption, eosinophilic degenerate cells in pituitary (males))

Relevant reproductive NOAEL ‡

≥ 5.33 mg/kg bw/day (no fertility effects)

Relevant offspring NOAEL ‡

5 mg/kg bw/day (reduced bw)

Developmental toxicity

Developmental target / critical effect ‡

Decreased foetal weight and retarded growth.

Relevant maternal NOAEL ‡

Rat: 4.7 mg/kg bw/day (reduced bw gain and food consumption)

Rabbit: 5 mg/kg bw/day (reduced bw gain)

Relevant developmental NOAEL ‡

Rat: 12.5 mg/kg bw/day (reduced bw, retarded ossification, no irreversible structural effects)

Rabbit: 15 mg/kg bw/day (no effects)

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡

NOAEL = 50 mg/kg bw (piloerection, hypoactivity, tremors and partially closed eyes, and in the FOB: lower activity (males), several reduced reflexes, reduced body temperature (females))

Repeated neurotoxicity ‡

NOAEL = 8.5 mg/kg bw/day (reduced bw gain and food consumption)

Delayed neurotoxicity ‡

No data-not required

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡

Body function tests: a.o. effects on activity, respiration rate, blood pressure, heart rate at 30 mg/kg bw (single dose).

Studies performed on metabolites or impurities ‡

Studies with PB-7: LD50 oral ≥2728 mg/kg bw, non-genotoxic in Ames test and lethal DNA damage test.

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Medical data ‡ (Annex IIA, point 5.9)

No evidence of adverse effects in workers; no data are available for consumers.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw/day	all semichronic and chronic studies	100
AOEL ‡	0.002 mg/kg bw/day	all semichronic and chronic studies	100 (+20% oral absorption)
ARfD ‡	0.05mg/kg bw	rabbit, developmental study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation

High dose (4.77 mg/cm²): 0.4%

Low dose (2.3 µg/cm²): 1.2%

Based on *in vitro* and *in vivo* dermal absorption studies with Nexter Pro.

Exposure scenarios (Annex IIIA, point 7.2)

Operator

Safe use was identified for operators with PPE (gloves, coverall, broad-rimmed headgear) for mechanical upward spraying on citrus, using the German model (67% of AOEL).

Safe use was identified for operators without PPE for manual up- and downward spraying on tomato, using the Dutch Glasshouse model (61% of AOEL).

Workers

Safe use was identified for workers without PPE during re-entry activities in citrus, using the EUROPOEM II (30% of AOEL).

Safe use was identified for workers with PPE during re-entry activities in tomato, using EUROPOEM II model (22% of AOEL).

Bystanders

Safe use was identified for bystanders for mechanical upward spraying on citrus, using the EUROPOEM II model (36% of AOEL).

Bystanders should not be allowed in greenhouses.

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

Substance classified (pyridaben)

RMS/peer review proposal

T "Toxic"**R23** "Toxic by inhalation"**R25** "Toxic if swallowed"

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Chapter 2.4 Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	Fruits (citrus, apple, tomato) (leaf-paint, fruit-paint and spray applications)
Rotational crops	Wheat, mustard, radish, swiss chard, sorghum
Metabolism in rotational crops similar to metabolism in primary crops?	Low total residues in rotational crops. Triggers for metabolite identification were not exceeded.
Processed commodities	Conditions simulating baking, brewing and sterilisation
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Pyridaben residues are stable upon processing.
Plant residue definition for monitoring	Pyridaben
Plant residue definition for risk assessment	Pyridaben
Conversion factor (monitoring to risk assessment)	1

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Goat, hen
Time needed to reach a plateau concentration in milk and eggs	milk: 2-3 days. eggs: >8 days.
Animal residue definition for monitoring	No definition of the residue in animal products is required
Animal residue definition for risk assessment	No definition of the residue in animal products is required
Conversion factor (monitoring to risk assessment)	None.
Metabolism in rat and ruminant similar (yes/no)	Yes.
Fat soluble residue: (yes/no)	No. (LogPow >3 but from livestock feeding studies pyridaben in fat will be <LOQ (0.05 mg/kg) at relevant intake levels).

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

No studies submitted and no studies required.

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Pyridaben is stable for up to 12 months in whole oranges, dried orange pulp, orange molasses and orange oil during frozen storage (<-5°C) and in apple and grapes for up to 12 months at -20°C.

Pyridaben is stable for up to 5 months in beef muscle,

beef liver and milk during frozen storage (<-5°C).

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)

Potential for accumulation (yes/no):

Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)

Muscle

Liver

Kidney

Fat

Milk

Eggs

Ruminant:	Poultry:	Pig:
Conditions of requirement of feeding studies		
yes, 0.17 mg/kg dw diet ¹	no	no
yes	-	-
no	-	-
Feeding studies (cows: 2.5 mg/kg dm feed) Residue levels in matrices : Mean (max) mg/kg		
<0.05	-	-
<0.05	-	-
<0.05	-	-
<0.05	-	-
<0.01		
	-	

¹ provisional calculation. Pending on the generation of new residue data under least favourable conditions.

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses	Recommendation/comments	MRL estimated from trials according to the representative use	HR	STMR
Tomato	NE + SE, Glasshouse	no	trials not performed under least favourable conditions	-	-	-
Oranges	SE	no	trials not performed under least favourable conditions	-	-	-
Mandarins	SE	no	trials not performed under least favourable conditions	-	-	-
Lemons	SE	no	trials not performed under least favourable conditions	-	-	-

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.01 mg/kg bw/d
TMDI (% ADI) according to WHO European diet	2.1%
TMDI (% ADI) according to national (to be specified) diets	9.1% (UK adults) 35.4% (UK toddlers)
IEDI (WHO European Diet) (% ADI)	Not necessary since TMDI < 100%
NEDI (specify diet) (% ADI)	Not necessary since TMDI < 100%
Factors included in IEDI and NEDI	
ARfD	0.05 mg/kg bw/d
IESTI (% ARfD)	1.5% (WHO-EU, orange)
NESTI (% ARfD) according to national (to be specified) large portion consumption data	5.8% (UK adults, orange) 23,8 (UK-toddlers, orange)
Factors included in IESTI and NESTI	Not necessary since IESTI/NESTI < 100%

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Washed oranges	3	0.49, 0.37, 0.66	na	
Juice	3	<0.1, <0.12, 0.14	na	
Wet pomace	3	0.75, 1.05, 1.11	na	
Molasses	1	0.30	na	
Dry pomace	3	3.5, 3.6, 5.2	na	
Orange oil	1	25.3	na	
Canned fruit	2	<0.04, <0.12		
Marmalade	2	<0.12, 0.21	na	

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Proposed MRLs	orange	0.2 mg/kg
	tomato	0.1 mg/kg

Chapter 2.5 Fate and Behaviour in the Environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡

18-20% after 90-120 d [benzene-U-¹⁴C] pyridaben (n=1)
0.1-12.8% after 90-120 d [pyridazinone-3,6-¹⁴C] pyridaben (n=4)

Non-extractable residues after 100 days ‡

12-16% after 90-120 d [benzene-U-¹⁴C] pyridaben (n=1)
15-31% after 90-120 d [pyridazinone-3,6-¹⁴C] pyridaben (n=4)

Metabolites requiring further consideration ‡
- name and/or code, % of applied (range and maximum)

PB-4 – max 7.6% at 150 d (n=4)
PB-7 – max 8.5% at 60 d (n=4)

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡

Mineralization after 100 days

no reliable data submitted (not required)

Non-extractable residues after 100 days

no reliable data submitted (not required)

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)

no reliable data submitted (not required)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)

PB-22
(max 13% in irradiated soil, not detected in dark soil)

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies ‡

Parent	Aerobic conditions - persistence endpoints						
Soil type	X ¹	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	DT ₅₀ (d) 20°C	St. (r ²)	Method of calculation
sandy loam 1 ²		6.2	20°C / 40% mwhc	132 / 597	132	1.00	DFOP
sandy loam 1 ³		6.2	20°C / 40% mwhc	181 / 778	181	0.99	DFOP
mean					157		
clay loam		7.6	20°C / 40% mwhc	50 / 241	50	0.99	DFOP
silt loam		6.7	20°C / 40% mwhc	199 / 4522	199	0.96	FOMC
sandy loam 2		6.0	20°C / 40% mwhc	80 / 2057	80	1.00	DFOP
sandy loam 2		6.0	10°C / 40% mwhc	279 / 926	- / - ⁴	0.93	SFO
Geometric mean/median/mean ⁵					106.6/118 / 121		

¹ X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

² Treatment with benzene-labeled 14C-pyridaben.

³ Treatment with pyridazinone-labeled 14C-pyridaben.

⁴ Not calculated since in the same soil a DT50 at 20°C was determined.

⁵ Calculated from the mean DT50 for the two labels of sandy loam 1, and the DT50 values at 20°C for the remaining three soils.

Laboratory studies ‡

Parent	Aerobic conditions – modelling endpoints						
Soil type	X ¹	pH	t. °C / % MWHC	DT ₅₀ (d)	DT ₅₀ (d) 20°C pF 2/10 kPa	St. (r ²)	Method of calculation
sandy loam 1 ²		6.2	20°C / 40% mwhc	135		0.95	SFO
sandy loam 1 ³		6.2	20°C / 40% mwhc	181		0.90	SFO
mean				158	106.4		
clay loam		7.6	20°C / 40% mwhc	65	37.6	0.95	SFO
silt loam		6.7	20°C / 40% mwhc	171	104.1	0.94	SFO
sandy loam 2		6.0	20°C / 40% mwhc	95.0	63.9	0.98	SFO
sandy loam 2		6.0	10°C / 40% mwhc	279	- / - ⁴	0.93	SFO
Geometric mean/median/mean ⁵					71.8/84.0/78.0		

¹ X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

² Treatment with benzene-labeled 14C-pyridaben.

³ Treatment with pyridazinone-labeled 14C-pyridaben.

⁴ Not calculated since in the same soil a DT50 at 20°C was determined.

⁵ Calculated from the mean DT50 for the two labels of sandy loam 1, and the DT50 values at 20°C for the remaining three soils.

Field studies ‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X ¹	pH	Depth (cm)	DT ₅₀ (d) actual	DT ₉₀ (d) actual	St. (r ²)	DT ₅₀ (d) Norm.	Method of calculation
sand, bare	Denmark		5.7	0-30	31	186	0.94	-	FOMC
sandy loam, bare	Denmark		6.1	0-30	36	160	0.96	-	DFOP
clay loam, bare	Spain ²		7.2	0-30	5.0	98	0.96	-	DFOP
sandy loam, bare	Spain ³		8.2	0-30	128	424	0.80	-	SFO
Geometric mean/median/mean					29/34/50	188/173 /217			

¹ X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

² Spring application.

³ Autumn application.

pH dependence ‡
(yes / no) (if yes type of dependence)

No

Soil accumulation and plateau concentration
‡

No data. Not required.

Laboratory studies ‡

Parent	Anaerobic conditions (no acceptable data provided, not required)
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Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH (water)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
sandy loam	0.31	7.3	-	-	108	34858	0.92
silt loam	0.42	7.0	-	-	330	78683	1.03
silt loam	0.25	5.2	-	-	220	87918	0.96
sand	0.69	5.5	-	-	445	64551	0.90
clay loam	0.31	6.2	-	-	6659	- ¹	1.28
Arithmetic mean						66503 /	0.953 ² /
median						71617	0.940 ²
pH dependence, Yes or No				No			

¹ Sorption was much higher than expected on the basis of the organic carbon content, which may be explained by the high clay and in particular smectite content, and therefore no Koc was calculated.

² Excluding the value for the clay loam.

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡

No study submitted. No data required.

Aged residues leaching ‡

No study submitted. No data required.

Lysimeter/ field leaching studies ‡

No study submitted. No data required.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

DT₅₀ (field): 36 d (Europe-N) and 128 d (Europe-S)

Method of calculation

Kinetics: DFOP for Europe-N (model parameters: $g = 0.515924$, $k_1 = 0.435319$, $k_2 = 0.00985516$); SFO for Europe-S.

Worst case DT50 from field studies.

Application data

Crop: **tomato (NE & SE) & citrus (SE)**

Depth of soil layer: 5 cm.

Soil bulk density: 1.5 g/cm³

% plant interception: 80% (tomato) & 70% (citrus)

Number of applications: 1

Application rate(s): 250 g a.s./ha (tomato)

300 g a.s./ha (citrus)

Tomato (Northern Europe)

PEC_(s) (mg/kg)	Single application	Single application	Multiple application	Multiple application
	Actual	Time weighted average	Actual	Time weighted average
Initial	0.067		x	
Short term 24h	0.054	0.060	x	x
2d	0.046	0.055	x	x
4d	0.037	0.048	x	x
Long term 7d	0.032	0.042	x	x
21d	0.026	0.033	x	x
28d	0.024	0.031	x	x
50d	0.020	0.027	x	x
100d	0.012	0.021	x	x
Plateau concentration (maximum/mean)				0.077 / 0.034

Tomato (Southern Europe)

PEC_(s) (mg/kg)	Single application	Single application	Multiple application	Multiple application
	Actual	Time weighted average	Actual	Time weighted average
Initial	0.067		x	
Short term 24h	0.066	0.066	x	x
2d	0.066	0.066	x	x
4d	0.065	0.066	x	x
Long term 7d	0.064	0.065	x	x
21d	0.060	0.063	x	x
28d	0.057	0.062	x	x
50d	0.051	0.058	x	x
100d	0.039	0.051	x	x
Plateau concentration (maximum/mean)				0.077 / 0.034

Citrus (Southern Europe)

PEC_(s) (mg/kg)	Single application	Single application	Multiple application	Multiple application
	Actual	Time weighted average	Actual	Time weighted average
Initial	0.120		x	
Short term 24h	0.119	0.120	x	x
2d	0.119	0.119	x	x
4d	0.117	0.119	x	x
Long term 7d	0.116	0.118	x	x
21d	0.107	0.113	x	x
28d	0.103	0.111	x	x
50d	0.092	0.105	x	x
100d	0.070	0.093	x	x
Plateau concentration (maximum/mean)				0.139 / 0.061

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡

Photolytic degradation of active substance and metabolites above 10 % ‡

Quantum yield of direct phototransformation in water at $\lambda > 290$ nm

Readily biodegradable ‡
(yes/no)

Hydrolytically stable at pH 5.0, pH 7.0 and pH 9.0 and 25° C.

The DT50 for aquatic photolysis of pyridaben at 25°C (Xenon light, 425 W/m²) is 6.8 minutes.

Major photodegradates:

W-1 (max. 27.9% AR, DT50 <1.5 hours);

B-3 (max. 29.2% AR, photolytically stable).

0.0304 mole/Einstein at 20°C

Not readily biodegradable in a modified Sturm test

Degradation in water / sediment

Parent	Persistence endpoints									
	Distribution (max in water 71.7% after 0 d. Max. in sediment 55.1% after 2 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT ₅₀ -DT ₉₀ whole sys.	St. (r ²)	DT ₅₀ -DT ₉₀ water ¹	St. (r ²)	DT ₅₀ -DT ₉₀ sed ¹	St. (r ²)	Method of calculation
silty clay ³	8.1	6.0	20	28.8-985	0.93	7.7-25.4	0.80	49.4-1245	0.94	HS/SFO/HS
silty clay ²	8.1	6.0	20	31.1-210	0.91	0.39-16.2	1.00	51.7-172	0.90	FOMC/DFOP/SFO
sandy silt loam ³	7.2	5.6	20	7.0-3769	0.98	1.3-4.9	1.00	207-2340	0.93	FOMC/DFOP/HS
sandy silt loam ²	7.2	5.6	20	14.9-278	0.87	0.49-4.9	0.99	118-392	0.62	DFOP/FOMC/SFO
Geometric mean				17.5-682		1.18-10.0		88.9-666		
Median				21.9-632		0.90-10.6		84.9-819		
Mean				20.5-1311		2.47-12.9		107-1037		

¹ half-lives for dissipation

² Treatment with benzene-labeled 14C-pyridaben.

³ Treatment with pyridazinone-labeled 14C-pyridaben.

WARNING: This document forms part of an MRL evaluation data package and should not be used for registration. Registration must not be granted on the basis of this document.

Parent	Modelling endpoints									
Water / sediment system	pH water phase	pH sed	t. °C	DT ₅₀ whole sys.	St. (r ²)	DT ₅₀ water	St. (r ²)	DT ₅₀ sed	St. (r ²)	Method of calculation
silty clay ²	8.1	6.0	20	651	0.93	651	-	651	-	HS
silty clay ¹	8.1	6.0	20	38.9	0.89	38.9	-	38.9	-	SFO
sandy silt loam ²	7.2	5.6	20	72.0	0.96	72.0	-	72.0	-	DFOP
sandy silt loam ¹	7.2	5.6	20	113	0.87	113	-	113	-	DFOP
Geometric mean				120		120		120		
Median				93		93		93		
Mean				219		219		219		

¹ Treatment with benzene-labeled 14C-pyridaben.² Treatment with pyridazinone-labeled 14C-pyridaben.

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d	Non-extractable residues in sed. Max x % after n d (end of the study)
silty clay ²	8.1	6.0	6.2% after 120 d		max 47.4% after 120 d
silty clay ¹	8.1	6.0	5.3% after 90 d (3.7% after 120 d)		max 38.0% after 120 d
sandy silt loam ²	7.2	5.6	0.1% after 120 d	max 40.0% after 59 d	39.3% after 120 d
sandy silt loam ¹	7.2	5.6	8.2% after 90 d (5.0% after 120 d)	max 38.9% after 59 d	34.0% after 120 d

¹ Treatment with benzene-labeled 14C-pyridaben.² Treatment with pyridazinone-labeled 14C-pyridaben.

Metabolites >10% in water or sediment					
Water / sediment system	pH water phase	pH sed	Metabolite	Maximum in water. Max x % after n d	Maximum in sediment. Max x % after n d
silty clay ²	8.1	6.0	PB-7	max 17.2% after 59 d	max 13.7% after 90 d
silty clay ¹	8.1	6.0	PB-7	max 15.3% after 59 d	max 14.1% after 120 d
sandy silt loam ²	7.2	5.6	PB-7	max 5.8% after 14 d	max 11.8% after 59 d

sandy silt loam ¹	7.2	5.6	PB-7	max 9.5% after 7 d	max 14.0% after 90 d
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¹ Treatment with benzene-labeled 14C-pyridaben.

² Treatment with pyridazinone-labeled 14C-pyridaben.

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Parent

Parameters used in FOCUSsw step 1 and 2

Version control no. of FOCUS calculator: vs 1.1
Molecular weight (g/mol): 364.9
Water solubility (mg/L): 0.012 (24°C)
K_{OC} (L/kg): 66503
DT₅₀ soil (d): 132.6 (conservative estimate used for PEC calculations, revised value is 71.8 days)
DT₅₀ water/sediment system (d): 218.7
DT₅₀ water (d): 218.7
DT₅₀ sediment (d): 218.7

Parameters used in FOCUSsw step 3 (if performed)

MACRO in FOCUS vs 4; PRZ in FOCUS vs 1; TOXSWA in FOCUS vs 2.4.2
DT₅₀ water/sediment system (d): 218.7
DT₅₀ water (d): 218.7
DT₅₀ sediment (d): 1000
K_{OC} (L/kg): 66503
1/n: 0.953

Application rate

Crop: fruiting vegetables (tomato) and citrus
Crop interception: average crop cover (50%) (tomato, NE & SE) and 70% (citrus, SE) (STEP 2)
Number of applications: 1
Application rate(s): 250 (tomato, NE & SE) and 300 g as/ha (citrus, SE)
Application window: January, May & October (Citrus, SE, representative of all year round use) (STEP 3)

FOCUS STEP 2 Scenario	Day after overall maximum	PEC _{SW} (µg/L)		PEC _{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Tomato, NE & SE GAP ¹	0 h	0.0833		0.6026	
	24 h	0.0283	0.0558	0.6023	0.6024
	2 d	0.0102	0.0375	0.6009	0.6020
	4 d	0.0023	0.0214	0.5973	0.6005
	7 d	0.0014	0.0129	0.5917	0.5979
	14 d	0.0013	0.0071	0.5787	0.5916
	21 d	0.0013	0.0052	0.5660	0.5851
	28 d	0.0013	0.0042	0.5536	0.5788
	42 d	0.0012	0.0032	0.5295	0.5664

¹ STEP 1 not applicable for greenhouse applications; to mimic this scenario, inputs through runoff and drainage were set equal to zero.

FOCUS STEP 3 ¹ Scenario	Day after overall maximum	PEC _{SW} (µg/L)		PEC _{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
CITRUS, SE GAP, January, D6 ditch	0 h	10.402		58.824	
	24 h	5.207	6.482	58.694	58.812
	2 d	4.192	5.577	58.353	58.777
	4 d	3.204	4.616	57.251	58.637
	7 d	2.356	3.820	55.068	58.269
	14 d	1.257	2.779	49.652	56.829
	21 d	0.761	2.179	44.975	54.929
	28 d	0.512	1.791	35.677	52.894
	42 d	0.019	1.237	27.860	47.590

CITRUS, SE GAP, January, R4 stream	0 h	7.820		15.982	
	24 h	0.018	1.102	6.903	9.962
	2 d	0.006	0.556	5.803	8.183
	4 d	0.002	0.280	4.998	6.784
	7 d	0.001	0.160	4.505	6.114
	14 d	0.000	0.080	4.029	6.009
	21 d	0.000	0.054	3.798	5.931

	28 d	0.000	0.040	3.646	5.861
	42 d	0.000	0.027	3.426	5.782
CITRUS, SE GAP, May, D6 ditch	0 h	10.402		57.757	
	24 h	5.187	6.470	57.613	57.744
	2 d	4.162	5.558	57.241	57.706
	4 d	3.163	4.589	56.047	57.555
	7 d	2.307	3.785	53.694	57.154
	14 d	1.213	2.737	47.893	55.595
	21 d	0.725	2.138	42.905	53.540
	28 d	0.483	1.752	38.554	51.346
	42 d	0.255	1.285	32.015	47.092
CITRUS, SE GAP, May, R4 stream	0 h	7.736		11.320	
	24 h	0.011	0.883	3.091	8.574
	2 d	0.003	0.445	2.233	8.530
	4 d	0.001	0.223	1.603	8.476
	7 d	0.000	0.128	1.221	8.424
	14 d	0.065	0.069	2.525	8.350
	21 d	0.000	0.052	5.564	8.339
	28 d	0.000	0.039	5.285	8.301
	42 d	0.000	0.026	4.873	8.215

CITRUS, SE GAP, October, D6 ditch	0 h	10.402		57.910	
	24 h	5.190	6.472	57.771	57.897
	2 d	4.166	5.561	57.405	57.859
	4 d	3.169	4.593	56.227	57.710
	7 d	2.314	3.790	53.900	57.314
	14 d	1.219	2.743	48.153	55.772
	21 d	0.730	2.144	43.209	53.740
	28 d	0.487	1.757	39.372	51.568
	42 d	0.267	1.292	33.713	47.510
CITRUS, SE GAP, October, R4 stream	0 h	7.165		14.784	
	24 h	0.001	0.331	14.316	14.506
	2 d	0.000	0.166	14.147	14.376
	4 d	0.000	0.086	13.928	14.211
	7 d	0.000	0.052	13.740	14.052
	14 d	0.001	0.037	13.421	13.817

	21 d	0.000	0.027	13.172	13.645
	28 d	0.000	0.021	12.955	13.502
	42 d	0.000	0.014	12.586	13.259

1 STEP 1 and 2 STEP 1 and STEP 2 calculations resulted in PEC_{sw} concentrations of pyridaben (15.7-16.8 µg/L) exceeding the water solubility of 12 µg/L. Therefore STEP 3 calculations were performed for pyridaben.

Metabolite PB-7

Parameters used in FOCUS_{sw} step 1 and 2

Molecular weight (g/mol): 394.9

Because no half-lives for PB-7 could be calculated, no PEC_{sw} calculations were performed according to FOCUS STEP 1 or 2. A rough indication of the maximum concentration was obtained by multiplying the T=0 results for pyridaben (STEP 1 for citrus, STEP 2 for tomato) with the maximum % of occurrence of PB-7 in water (17%) or sediment (14%) and by applying a MW correction factor of 1.08 (i.e. 394.9/364.9).

FOCUS STEP 1 Scenario	Day after overall maximum	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg)	
		Actual	TWA	Actual	TWA
Citrus, SE GAP	0 h	3.0982	-	112.3653	-

FOCUS STEP 2 Scenario	Day after overall maximum	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg)	
		Actual	TWA	Actual	TWA
Tomato, NE & SE GAP	0 h	0.0153	-	0.0913	-

Metabolite W-1

Parameters used in FOCUS_{sw} step 1 and 2

Molecular weight (g/mol): 328.5

Because no half-lives for W-1 could be calculated, no PEC_{sw} calculations were performed according to FOCUS STEP 1 or 2. A rough indication of the maximum concentration was obtained by multiplying the T=0 results for pyridaben (STEP 1 for citrus, STEP 2 for tomato) with the maximum % of occurrence of PB-7 in water or sediment and by applying a MW correction factor of 0.90 (i.e. 328.5/364.9). The maximum % of occurrence in the aqueous photolysis study was either completely attributed to the water or to the sediment phase.

FOCUS STEP 1 Scenario	Day after overall maximum	PEC _{SW} (µg/L)		PEC _{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Citrus, SE GAP	0 h	4.2286	-	186.2248	-

FOCUS STEP 2 Scenario	Day after overall maximum	PEC _{SW} (µg/L)		PEC _{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Tomato, NE & SE GAP	0 h	0.0209	-	0.1513	-

Metabolite B-3

Parameters used in FOCUS_{sw} step 1 and 2

Molecular weight (g/mol): 164.3

Because no half-lives for B-3 could be calculated, no PEC_{sw} calculations were performed according to FOCUS STEP 1 or 2. A rough indication of the maximum concentration was obtained by multiplying the T=0 results for pyridaben (STEP 1 for citrus, STEP 2 for tomato) with the maximum % of occurrence of PB-7 in water or sediment and by applying a MW correction factor of 0.45 (i.e. 164.3/364.9). The maximum % of occurrence in the aqueous photolysis study was either completely attributed to the water or to the sediment phase.

FOCUS STEP 1 Scenario	Day after overall maximum	PEC _{SW} (µg/L)		PEC _{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Citrus, SE GAP	0 h	2.2128	-	97.4510	-

FOCUS STEP 2 Scenario	Day after overall maximum	PEC _{SW} (µg/L)		PEC _{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Tomato, NE & SE GAP	0 h	0.0109	-	0.0792	-

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)

Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance.

Model used: FOCUS-PEARL 2.2.2

Scenarios: All FOCUS scenarios

Crop: citrus

Geometric mean parent DT_{50lab} 71.8 d (normalisation to 10kPa or pF2, 20°C).

K_{OC} : parent, arithmetic mean 66503, $1/n = 0.953$.

Metabolites: PB-4

Geometric mean metabolite DT_{50lab} 1000 d (no experimental value available).

K_{OC} metabolite 71490, $1/n = 0.9$ (default).

Application rate

Application rate: 300 g a.s./ha (SE)

No. of applications: 1

Time of application: January, April & October (representative of all year round use)

Crop interception: 70%

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1 m)

Citrus / Southern EU GAP	FOCUS-PEARL 2.2.2	Scenario	Parent (µg/L)	Metabolite (µg/L)		
				PB-4	2	3
		Chateaudun	n.a.	n.a.	-	-
		Hamburg	n.a.	n.a.	-	-
		Jokioinen	n.a.	n.a.	-	-
		Kremsmunster	n.a.	n.a.	-	-
		Okehampton	n.a.	n.a.	-	-
		Piacenza	< 0.001	< 0.001	-	-
		Porto	< 0.001	< 0.001	-	-
		Sevilla	< 0.001	< 0.001	-	-
		Thiva	< 0.001	< 0.001	-	-

n.a. = not applicable

tomato / Europe N & S GAP FOCUS-PEARL 2.2.2	Scenario	Parent (µg/L)	Metabolite (µg/L)		
			PB-4	2	3
	Dutch spring	<0.001	<0.001	-	-

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡

Not studied - no data requested

Quantum yield of direct phototransformation

Not studied - no data requested

Photochemical oxidative degradation in air ‡

DT₅₀ of 4.8 hours derived by the Atkinson model. OH (12 h) concentration assumed = 9.7×10^5 OH/cm³

Volatilisation ‡

Henry's Law Constant 0.304 Pa.m³.mol⁻¹ (24°C)

Metabolites

Estimated values using the models EPISUITE and AOPWIN:

- Vapour pressure : PB-22: 6.3E-13 Pa; B-3: 0.157 Pa; PB-7: 2.87E-9 Pa
- Water solubility at 25°C : PB-22: 166.8 mg/l; B-3: 97.8 mg/l; PB-7: 1.65 mg/l
- Henry's law constant : PB-22: 1.5×10^{-17} atm-m³/mol; B-3: 4.3×10^{-7} atm-m³/mol; PB-7: 6.8×10^{-12} atm-m³/mol
- Atmospheric oxidation half-life : PB-22: 1.0 days; B-3: 1.1 days; PB-7: 7.0 days

PEC (air)

Method of calculation

Expert judgement; based on vapour pressure, dimensionless Henry's Law Constant, Atkinson calculation and laboratory volatility studies, no residues of pyridaben and metabolites in air are expected.

PEC(a)

Maximum concentration

No data provided - none requested

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).

Soil:	active substance and PB-22
Surface Water:	active substance, PB-7, W-1, B-3
Sediment:	active substance, PB-7
Ground water:	PB-4 and PB-22 ¹
Air:	active substance, PB-22, PB-7 and B-3

¹ No leaching to groundwater of parent pyridaben and major soil metabolite PB-7 is expected to occur.

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	No data provided - none requested
Surface water (indicate location and type of study)	No data provided - none requested
Ground water (indicate location and type of study)	No data provided - none requested
Air (indicate location and type of study)	No data provided - none requested

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Not readily biodegradable

Chapter 2.6 Ecotoxicology

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds				
Mallard duck	a.s.	Acute	LD50: >2500	-
Bobwhite quail	a.s.	Acute	LD50: >2250	-
Mallard duck	a.s.	Short-term	NOEC: 659 ¹	NOEC: 3160 ¹
Bobwhite quail	a.s.	Short-term	LC50: >4298	LC50: >5620
Mallard duck	a.s.	Long-term	NOEC: 10	NOEC: 100
Bobwhite quail	a.s.	Long-term	NOEC: 130	NOEC: 1000
Mammals				
Rat	a.s.	Acute	LD50: 161 ²	-
Rat	a.s.	Acute	LD50: 570 ³	-
Rat	a.s.	Long-term	NOEC: 1.87	NOEC: 28
Additional higher tier studies ‡				
No data available – not required				

¹ The dietary LC50 could not be recalculated into mg/kg bw/day. The NOEC for mortality is used instead

¹ Pyridaben suspended in maize oil

² Pyridaben suspended in aqueous carboxymethyl cellulose

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Citrus 0.30 kg a.s./ha (worst-case exposure)

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Route: insects	Acute	16	139	10
Route: surface water	Acute	0.0028	8E+05	10
Route: puddle water	Acute	21.6	>104	10
Route: insects	Short-term	9.0	73	10
Route: insects	Long-term	9.0	1.1	5
Route: earthworms	Long-term	>2.3	<4.4	5
Route: fish	Long-term	<0.02	>464	5
Tier 1 (Mammals)				
Route: grasses	Acute	18	324 ¹	10
Route: surface water	Acute	0.0016	1E+05	10
Route: puddle water	Acute	12.8	12.6	10

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Route: grasses	Long-term	5.0	0.37	5
Route: earthworms	Long-term	>2.8	<0.67	5
Route: fish	Long-term	<0.014	>138	5

¹ based on the LD50 in aqueous carboxymethyl cellulose

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	End point	Toxicity ¹ (µg/L)
Laboratory tests				
Fish				
<i>Oncorhynchus mykiss</i>	a.s.	96 hr (flow-through)	Mortality, LC ₅₀	0.73 _(mm)
	Preparation (Pyridaben 75WP)	96 hr (semi-static)	Mortality, LC ₅₀	2.2 _(a.s., mm)
	PB-7	96 hr (semi-static)	Mortality, LC ₅₀	>8000 _(mm)
<i>Lepomis macrochirus</i>	a.s.	96 hr (flow-through)	Mortality, LC ₅₀	3.5 _(mm)
	Preparation (BAS 300 11 f)	96 hr (static outdoors)	Mortality, LC ₅₀	64 _(a.s., initial)
<i>Cyprinodon variegatus</i>	a.s.	96 hr (flow-through)	Mortality, LC ₅₀	17 _(mm)
<i>Pimephales promelas</i>	a.s.	301 d (flow-through)	Fish full life cycle test, NOEC	0.28 _(mm)
Aquatic invertebrate				
<i>Daphnia magna</i>	a.s.	48 h (flow-through)	Mortality, LC ₅₀	1.0 _(mm)
	a.s.	21 d (flow-through)	Reproduction, NOEC	0.086 _(mm)
	Preparation (Pyridaben 75WP)	48 h (static)	Mortality, LC ₅₀	0.99 _(a.s., nom)
	PB-7	48 h (static)	Mortality, LC ₅₀	28 _(mm)
<i>Mysidopsis bahia</i>	a.s.	96 h (flow-through)	Mortality, LC ₅₀	0.67 _(mm)
	a.s.	35 d (flow-through)	Reproduction, NOEC	0.047 _(mm)

Group	Test substance	Time-scale (Test type)	End point	Toxicity ¹ (µg/L)
	Preparation (BAS 300 11 I)	96 h (static outdoors)	Mortality, LC ₅₀	16 (a.s., initial)
<i>Crassostrea virginica</i>	a.s.	96 h (flow- through)	Shell growth, EC ₅₀	8.3 (mm)
Sediment dwelling organisms				
<i>Chironomus riparius</i>	a.s.	28 d (static)	Emergence and development, NOEC	5.1 (initial)
<i>Chironomus riparius</i>	PB-7	48 h (static)	Mortality, LC ₅₀	140 (initial)
Algae				
<i>Selenastrum capricornutum</i>	a.s.	72 h (static)	Biomass: E _b C ₅₀ Growth rate: E _r C ₅₀	>17 (initial) >17 (initial)
	Preparation (Pyridaben 75WP)	72 h (static)	Biomass: E _b C ₅₀ Growth rate: E _r C ₅₀	35000 (a.s., nom) 68000 (a.s., nom)
	PB-7	72 h (static)	Biomass: E _b C ₅₀ Growth rate: E _r C ₅₀	3100 (initial) >16000 (initial)
<i>Anabaena flos-aquae</i>	a.s.	120 h (static)	Biomass: E _b C ₅₀ Growth rate: E _r C ₅₀	>13 (initial) >13 (initial)
<i>Navicula pelliculosa</i>	a.s.	120 h (static)	Biomass: E _b C ₅₀ Growth rate: E _r C ₅₀	>14 (initial) >14 (initial)
<i>Skeletonema costatum</i>	a.s.	120 h (static)	Biomass: E _b C ₅₀ Growth rate: E _r C ₅₀	>16 (initial) >16 (initial)
Higher plant				
No reliable data submitted – no data required				

Microcosm or mesocosm tests				
Phytoplankton, zooplankton, periphyton, macroinvertebrates and fish (bluegill)	Preparation (BAS 300 11 I)	12 weeks	Microcosm, NOEC	<0.34 (a.s., initial, 2 applications at 29 days' interval)
			Microcosm, EAC	0.11 (a.s., initial, 2 applications at 29 days' interval)

In microcosms containing sediment and treated with pyridaben, no treatment related mortality of fish (bluegill sunfish) was observed after 56 days at a simulated spray drift application (nominal treatment rate 1.7 µg a.s./L) followed by a simulated runoff treatment 20 hours later (nominal treatment rate 2.0 µg a.s./L).

¹ indicate whether based on nominal (_{nom}) or mean measured concentrations (_{mm}). In the case of preparations indicate whether end points are presented as units of preparation or a.s.

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

FOCUS Step 2 (FOCUS Step 1 is not considered appropriate for greenhouse treatments)

Tomato, 0.25 kg a.s./ha

Test substance	N/S ¹	Organism	Toxicity end point (µg/L)	Time scale	PEC _{sw} ² (max., µg/L)	TER	Annex VI Trigger
a.s.	N+S	Fish	0.73	Acute	0.0833	8.8	100
a.s.	N+S	Fish	0.28	Chronic	0.0833	3.4	10
a.s.	N+S	Aquatic invertebrates	0.67	Acute	0.0833	8.0	100
a.s.	N+S	Aquatic invertebrates	0.047	Chronic	0.0833	0.56	10
a.s.	N+S	Algae	35000	Acute	0.0833	4E+05	10
a.s.	N+S	Sediment organisms	5.1	Chronic	0.0833	61	10
PB-7	N+S	Fish	>8000	Acute	0.0153	>5E+05	100
PB-7	N+S	Aquatic invertebrates	28	Acute	0.0153	1830	100
PB-7	N+S	Algae	3100	Acute	0.0153	2E+05	10
PB-7	N+S	Sediment-dwelling organisms	150	Acute	0.0153	9804	100

¹ indicate whether Northern or Southern

² indicate whether maximum or two values have been used.

Citrus, 0.30 kg a.s./ha

Test substance	N/S ¹	Organism	Toxicity end point (µg/L)	Time scale	PEC _{sw} ² (max., µg/L)	TER	Annex VI Trigger
PB-7	N+S	Fish	>8000	Acute	3.0982	>2582	100
PB-7	N+S	Aquatic invertebrates	28	Acute	3.0982	9.0	100
PB-7	N+S	Algae	3100	Acute	3.0982	1001	10
PB-7	N+S	Sediment-dwelling organisms	150	Acute	3.0982	48	100

¹ indicate whether Northern or Southern

² indicate whether maximum or two values have been used.

FOCUS Step 3 (Step 1 and Step 2 calculations resulted in PEC_{sw} values > water solubility)

Citrus, 0.30 kg a.s./ha

Test substance	Scenario ¹	Water body type ²	Test organism	Time scale	Toxicity end point (µg/L)	PEC _{sw} (max., µg/L) ³	TER	Annex VI trigger
a.s.	D6	Ditch	Fish	Acute	0.73	10.402	0.070	100
a.s.	D6	Ditch	Fish	Chronic	0.28	10.402	0.027	10
a.s.	D6	Ditch	Aquatic invertebrates	Acute	0.67	10.402	0.064	100
a.s.	D6	Ditch	Aquatic invertebrates	Chronic	0.047	10.402	0.0045	10
a.s.	D6	Ditch	Algae	Acute	35000	10.402	3365	10
a.s.	D6	Ditch	Sediment organisms	Chronic	5.1	10.402	0.49	10
a.s.	R4	Stream	Fish	Acute	0.73	7.820	0.093	100
a.s.	R4	Stream	Fish	Chronic	0.28	7.820	0.036	10
a.s.	R4	Stream	Aquatic invertebrates	Acute	0.67	7.820	0.086	100
a.s.	R4	Stream	Aquatic invertebrates	Chronic	0.047	7.820	0.0060	10
a.s.	R4	Stream	Algae	Acute	35000	7.820	4476	10
a.s.	R4	Stream	Sediment organisms	Chronic	5.1	7.820	0.65	10

¹ drainage (D1-D6) and run-off (R1-R4)² ditch/stream/pond³ indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or two values used

WARNING: This document forms part of an EC evaluation data package and should not be relied upon as the basis of this document.

Registration must not be granted on the basis of this document.

Bioconcentration				
	Active substance	PB-7	W-1	B-3
logP _{OW}	>6.37	3.67 ² -3.86 ³	4.29 ³ -4.96 ²	2.94 ² -2.99 ³
Bioconcentration factor (BCF) ¹	<48 (pyridaben, 6% lipid)	No data submitted – no data required	No data submitted – no data required	No data submitted – no data required
Annex VI Trigger for the bioconcentration factor	100			
Clearance time (days) (CT ₅₀)	0.7-0.9			
(CT ₉₀)	2.4-3.0			
Level and nature of residues (%) in organisms after the 14 day depuration phase	<0.7%; nature not investigated			

¹ only required if log P_{OW} >3.

² estimated by Pallas 3.0 software

³ estimated by EPA EPI Suite software

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD ₅₀ µg/bee)	Acute contact toxicity (LD ₅₀ µg/bee)
a.s.	0.535	0.024
Preparation (formulated NC-129, SC formulation)	4.45 (a.s.)	0.691 (a.s.)
Preparation (Pyridaben 20WP formulation)	2.12 (a.s.)	3.68 (a.s.)
Tunnel tests		
BAS 9078 0 I (A) and BAS 9078 4 I (A): Based on mortality and foraging behaviour: NOEC <1.2 kg a.s./ha. Nexter: Based on mortality and bee brood development: NOEC <0.15 kg a.s./ha.		
Bee brood study		
Pyridaben 20 WP did not have an adverse effect on the development of the brood of honey bees at concentrations up to 100 mg a.s./L.		
Field or semi-field tests		
No acceptable data submitted – data required		

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Tomato, 0.25 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI trigger
a.s.	Contact	10417	50
a.s.	Oral	467	50

Citrus, 0.30 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI trigger
a.s.	Contact	12500	50
a.s.	Oral	561	50

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR ₅₀ g a.s./ha)
<i>Typhlodromus pyri</i>	Preparation (Pyridaben 75WP)	Mortality	0.59
<i>Aphidius rhopalosiphi</i>	Preparation (Pyridaben 75WP)	Mortality	0.24

Citrus, 0.30 kg a.s./ha

Test substance	Species	Effect (LR ₅₀ g/ha)	HQ in-field	HQ off-field	Trigger
Pyridaben 75 WP	<i>Typhlodromus pyri</i>	0.59	508	80	2
Pyridaben 75 WP	<i>Aphidius rhopalosiphi</i>	0.24	1250	197	2

Tomato, 0.25 kg a.s./ha

Test substance	Species	Effect (LR ₅₀ g/ha)	HQ in-field	HQ off-field	Trigger
Pyridaben 75 WP	<i>Typhlodromus pyri</i>	0.59	424	Not applicable	2
Pyridaben 75 WP	<i>Aphidius rhopalosiphi</i>	0.24	1042	Not applicable	2

Further laboratory and extended laboratory studies

Species	Life stage	Test type, substrate and duration	Dose (g a.s./ha)	Endpoint	effect (positive effect is adverse) and LR50 and ER50 values	Trigger Value
<i>Typhlodromus pyri</i>	Proto-nymphs	Preparation ¹ , extended laboratory, fresh residues on apple leaf discs, 14 days	47; 200; 300	Mortality	80; 96; 93	50%
				Reduction of reproduction	n.a. ² ; n.a. ² ; n.a. ² ER50 (g a.s./ha): <47	50%
		Preparation ¹ , extended laboratory, 7-day aged residues on apple leaf discs, 14 days	47; 200; 300	Mortality	86; 96; 99	50%
				Reduction of reproduction	n.a. ² ; n.a. ² ; n.a. ² ER50 (g a.s./ha): <47	50%
		Preparation ¹ , extended laboratory, 14-day aged residues on apple leaf discs, 14 days	47; 200; 300	Mortality	3.2; 56; 80	50%
				Reduction of reproduction	155 2; n.a. ² ; n.a. ² ER50 (g a.s./ha): >47	50%
		Preparation ¹ , extended laboratory, 21-day aged residues on apple leaf discs, 14 days	47; 200; 300	Mortality	1.1; 7.7; 46	50%
				Reduction of reproduction	LR50 (g a.s./ha): 300 1; 11; 17 ER50 (g a.s./ha): >300	50%
		Preparation ¹ , extended laboratory, 28-day aged residues on apple leaf discs, 14 days	300	Mortality	32	50%
				Reduction of reproduction	LR50 (g a.s./ha): >300 22 ER50 (g a.s./ha): >300	50%
<i>Aphidius rhopalosiphi</i>	Adults	Preparation ¹ , extended laboratory, fresh residues on apple leaves, 2 days	47; 200; 300	Mortality	92; 100; 100	50%
				Reduction of reproduction	LR50 (g a.s./ha): <47 n.a. ² ; n.a. ² ; n.a. ² ER50 (g a.s./ha): <47	50%
		Preparation ¹ , extended laboratory, 7-day aged residues on apple leaves, 2 days	47; 200; 300	Mortality	70; 100; 100	50%
				Reduction of reproduction	LR50 (g a.s./ha): <47 n.a. ² ; n.a. ² ; n.a. ² ER50 (g a.s./ha): <47	50%
<i>Aphidius rhopalosiphi</i>	Adults	Preparation ¹ , extended laboratory, 14-day aged residues on apple leaves, 2 days	47; 200; 300	Mortality	43; 98; 100	50%
				Reduction of reproduction	LR50 (g a.s./ha): 56 71; n.a. ² ; n.a. ² ER50 (g a.s./ha): <47	50%
		Preparation ¹ , extended laboratory, 21-day aged	47; 200; 300	Mortality	7.9; 68; 92	50%
					LR50 (g a.s./ha): 123	

Species	Life stage	Test type, substrate and duration	Dose (g a.s./ha)	Endpoint	effect (positive effect is adverse) and LR50 and ER50 values	Trigger Value
		residues on apple leaves, 2 days		Reduction of reproduction	0; 91; n.a. ² ER50 (g a.s./ha): 104	50%
		Preparation ¹ , extended laboratory, 28-day aged residues on apple leaves, 2 days	47; 200; 300	Mortality	13; 36; 82 LR50 (g a.s./ha): 172	50%
				Reduction of reproduction	52; 78; n.a. ² ER50 (g a.s./ha): 42	50%
		Preparation ¹ , extended laboratory, 35-day aged residues on apple leaves, 2 days	47; 200; 300	Mortality	0; 35; 74 LR50 (g a.s./ha): 208	50%
				Reduction of reproduction	8; 12; 70 ER50 (g a.s./ha): 261	50%
		Preparation ¹ , extended laboratory, 42-day aged residues on apple leaves, 2 days	200; 300	Mortality	18; 60 LR50 (g a.s./ha): 272	50%
<i>Chrysoperla carnea</i>	2 nd instar larvae			Reduction of reproduction	77; 32 ER50 (g a.s./ha): >300	50%
		Preparation ¹ , extended laboratory, 49-day aged residues on apple leaves, 2 days	200; 300	Mortality	42; 2.8 LR50 (g a.s./ha): >300	50%
				Reduction of reproduction	-144 ³ ; -103 ³ ER50 (g a.s./ha): >300	50%
<i>Chrysoperla carnea</i>	2 nd instar larvae	Preparation ⁴ , extended laboratory, fresh residues on field treated apple leaves, until adult emergence	53; 247; 308	Reduction of reproduction	6; -32 ³ ; -35 ³ ER50 (g a.s./ha): >308	50%
<i>Chrysoperla carnea</i>	2 nd instar larvae	Preparation ⁴ , extended laboratory, 15-day aged residues on field-treated apple leaves, until adult emergence	53; 247; 308	Reduction of reproduction	42; -4 ³ ; 36 ER50 (g a.s./ha): >308	50%

¹ Pyridaben 75WP = 750 g pyridaben/kg

² n.a. = not applicable (insufficient survivors from initial phase to assess reproduction).

³ Note: negative effect %, hence no adverse effect.

⁴ Nexter (BAS 300 11 I) = 750 g pyridaben/kg

Field or semi-field tests

No significant effects on non-target arthropod population in citrus orchard in Spain up to 47 g a.s./ha.

No significant effects on non-target arthropod population in apple orchard in France up to 39 g a.s./ha.

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point
Earthworms			
<i>Eisenia fetida</i>	a.s.	Acute 14 days	LC _{50,corr} : 19 mg a.s./kg soil
	Preparation (Pyridaben 75WP)	Acute 14 days	LC _{50,corr} : 42 mg a.s./kg soil
	Preparation (Pyridaben 75WP)	Chronic 8 weeks	NOEC: 0.29 mg a.s./kg soil (2.9% oc)
Field tests			
No acceptable data submitted – data required.			
Other soil macro-organisms			
Soil mite	No data submitted – no data required		
Collembola	Preparation (Pyridaben 75WP)	Chronic 28 days	NOEC: 3.28 mg a.s./kg (2.33% oc)
Soil micro-organisms			
Nitrogen mineralisation	a.s.		No data submitted – no data required
	Preparation (BAS 9087 6 I)	Chronic 28 days	Loamy sand soil: NOEC 8.0 mg a.s./kg soil
Carbon mineralisation	a.s.		No data submitted – no data required
	Preparation (BAS 9078 6 I)	Chronic 28 days	Sandy loam soil: NOEC 8.0 mg a.s./kg soil
Field studies			
Litter bag test: Soil litter degradation was not inhibited by two spray applications at 15-days interval of Pyridaben 75 WP at a nominal rate of 174 and 301 g a.s./ha (total measured dose 0.11 mg a.s./kg soil).			

Toxicity/exposure ratios for soil organisms

Citrus, 0.30 kg a.s./ha

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	a.s.	Acute	0.139	137	10
	a.s.	Chronic	0.139	2.1	5

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Other soil macro-organisms					
Collembola	Preparation (Pyridaben 75WP)	Chronic	0.139	24	5

Tomato, 0.25 kg a.s./ha

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	a.s.	Acute	0.077	247	10
	a.s.	Chronic	0.077	3.8	5
Other soil macro-organisms					
Collembola	Preparation (Pyridaben 75WP)	Chronic	0.077	43	5

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Preliminary screening data

Seedling emergence and vegetative vigor test in ten plant species, ≤23% effect on seedling emergence, survival, plant height and biomass at 0.56 kg a.s./ha (tomato, corn, soybean, lettuce, radish, cucumber, cabbage, oat, ryegrass and onion). *In vitro* seed germination not affected by more than 7% at 1.5 mg a.s./L.

Laboratory dose response tests

Most sensitive species	Test substance	ER ₅₀ (g/ha) vegetative vigour	ER ₅₀ (g/ha) emergence	Exposure (g/ha)	TER	Trigger
No data submitted – no data required						

Additional studies (e.g. semi-field or field studies)

No data submitted – no data required

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	end point
Activated sludge	3-hour EC ₅₀ >100 mg a.s./L
<i>Pseudomonas sp</i>	No data submitted – no data required

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)*

Compartment	
soil	Pyridaben and PB-22
water	Pyridaben, PB-7, W-1 and B-3
sediment	Pyridaben, PB-7
groundwater	No relevant compounds

* Detailed guidance to define the ecotoxicologically relevant compounds is not available. Provisionally therefore, the active substance and major metabolites are listed in the definition . See also section B.8.9.

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

Active substance

RMS/peer review proposal

N, R50/53

Preparation

RMS/peer review proposal

N, R50/53

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LEVEL 3

Pyridaben

PROPOSAL FOR THE DECISION

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3 Proposed decision with respect to the application for inclusion of the active substance in Annex I

3.1 Background to the proposed decision

Pyridaben is an insecticide and acaricide to be used in agriculture for the control of insects and mites on citrus orchards and greenhouse tomatoes and is orally and/or percutaneously taken into mobile forms of insects (whiteflies, aphids, mites) when treated via contact or residual. The representative formulation is a pyridaben 75WP formulation.

The identity of pyridaben is sufficiently described. With regard to physical and chemical properties certain questions need to be answered with a satisfactory result (see level 4).

The provided analytical methods for the determination of the a.s. in technical material and in the plant protection product are acceptable. Submitted methods supported LOQs of 0.05 mg/kg for orange fruit and orange process products and 0.05 mg/kg for tomato. No acceptable methods for products of animal origin were submitted. Since no residues are expected in animal products, further questions are redundant.

As pyridaben is classified as toxic, methods validated in blood and tissues are required. The method for the determination of pyridaben, PB-7 and PB-9 in animal products, which used a methylation step with diazomethane, is acceptable for pyridaben when the methylation step is excluded, except that a confirmatory method has not been provided. An acceptable method in blood with an LOQ of 0.05 mg/l was submitted.

Acceptable methods were submitted for determination of pyridaben in soil, water and air. However, additional methodology for all the metabolites included in the residue definitions for water, soil and air should be submitted.

An ADI for dietary exposure of 0.01 mg/kg bw/day was established. A systemic AOEL for chronic exposure, based on oral toxicity data, of 0.002 mg/kg bw/day can be set. An ARfD of 0.05 mg/kg bw/day is proposed.

Based on the AOEL and exposure assessments, for the pyridaben 75WP formulation safe uses have been identified for mechanical upward spraying on citrus and manual up- and downward spraying on tomato. A safe use has also been identified for re-entry activities in citrus and tomato. A safe use for bystanders has been identified for mechanical upward spraying on citrus. No bystanders should be allowed in greenhouses during the application of the pyridaben 75WP formulation on tomato.

The plant residue definition for risk assessment and monitoring is pyridaben. No definition of the residue in animal products is required. The TMDI (% ADI) according to WHO European diet is 2.1% and according to the UK diet 9.1% for adults and 35.4% for toddlers. The IESTI (% ARfD) according to the WHO European diet is 1.5% (orange) and according to the UK diet 5.8% (orange) for adults and 23.8% (orange) for toddlers. The proposed MRL is 0.2 mg/kg for orange and 0.1

mg/kg for tomato. The notifier is requested to provide 4 additional residue trials with mandarin according to cGAP for calculation of an MRL for mandarin and/or the whole group of citrus.

With regard to fate and behaviour, additional data are required to be able to make a complete assessment whether the conditions contained in Article 5(1) of Council Directive 91/414/EEC are satisfied.

The risk assessment for birds and mammals needs to be refined for the application in citrus. The risk assessment for aquatic invertebrates, fish, sediment-dwelling organisms, bees and earthworms needs to be refined for both applications. Therefore, additional data are required to be able to make a complete assessment whether the conditions contained in Article 5(1) of Council Directive 91/414/EEC are satisfied, in particular, further data on ecotoxicology.

3.2 Proposed decision concerning inclusion in Annex I

[REDACTED]

3.3 Rational for the postponement of the decision to include the active substance in Annex I, or for the conditions and restrictions to be associated with a proposed inclusion in Annex I, as appropriate

[REDACTED]

The information in sections 3.2 and 3.3 has been removed upon request by the EU Commission as it relates to risk management recommendations or proposals.

LEVEL 4

Pyridaben

DEMAND FOR FURTHER INFORMATION

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4 Further information to permit a decision to be made, or to support a review of the conditions and restrictions associated with the proposed inclusion in Annex I

4.1 Identity of the active substance

No further information is required.

4.2 Physical and chemical properties of the active substance

The following data is not available or insufficiently reliable and should be provided:

- The water solubility under GLP according to EEC A.6 and OECD 105 should be determined and a new Henry constant calculated.
- The report on the determination of flammability is to be supplemented with data on the purity of the substance.
- The report on the determination of explosive properties is to be supplemented with data on the purity of the substance.

Plant protection product: Pyridaben 75WP in WSB (750 g/kg Pyridaben)

The following data is not available and should be provided:

- Bags did not fully dissolve and blocked the test funnel in three out of four tests. A practical sprayability test showing acceptable dissolution in a spray tank must be performed (study is in progress).

4.3 Data on application and further information

No further information is required.

4.4 Classification, packaging and labelling

No further information necessary.

4.5 Methods of analysis

For the method in blood notifier is asked to confirm the fortification levels as in the chromatograms in the study the levels were different as stated in the text of the report. A confirmatory method should be provided for the determination of pyridaben in tissues.

Acceptable methods were submitted for determination of pyridaben in soil, water and air. Methods for the determination of all the metabolites included in the residue definitions for water, soil and air should be submitted (data gap). At this moment the final residue definition for soil, water and air still has to be decided on. Depending on the outcome the data requirements can change.

4.6 Toxicology and metabolism

No further information necessary.

4.7 Residue data

The notifier is requested to provide 4 additional residue trials with mandarin according to cGAP for calculation of an MRL for mandarin and/or the whole group of citrus.

4.8 Environmental fate and behaviour

The following information is required to permit a decision regarding inclusion in Annex I:

Fate and behaviour in soil

DT₅₀ values in three soils are required for the metabolite PB-7 and the photodegrade PB-22.

Fate and behaviour in soil

Koc values in three soils are required for the soil metabolite PB-7 and for the soil photodegrade PB-22.

Fate and behaviour in soil and water

PEC_{gw}, PEC_s, PEC_{sw} and PEC_{air} estimations employed a value for water solubility of pyridaben of 0.012 mg/L at 24°C. This value however was marked as insufficiently reliable (section B.2.2). In case a new value is submitted the need for revision of the PEC estimations should be considered.

Fate and behaviour in water

Koc values in three soils are required for the soil metabolite PB-7 and for the soil photodegrade PB-22.

4.9 Ecotoxicology

The following information is required to permit a decision regarding inclusion in Annex I:

1. Active substance: data for refined risk assessment of long-term exposure of birds to contaminated insects.
2. Active substance: data for refined risk assessment of long-term exposure of birds to contaminated earthworms.
3. Active substance: data for refined risk assessment of long-term exposure of mammals to contaminated earthworms.
4. Active substance: data for refined risk assessment of long-term exposure of mammals to contaminated grass.
5. Formulated product: data for refined risk assessment for aquatic invertebrates and sediment-dwelling organisms for the application in citrus (the smallest buffer zone at which the risk is acceptable is 225 m).
6. Formulated product: additional data for a refined risk assessment for fish for both applications.
7. PB-7: data to assess the acute risk of PB-7 to aquatic invertebrates for the application in citrus.
8. PB-7: data to assess the acute risk of PB-7 to sediment-dwelling organisms for the application in citrus.
9. Photodegradate W-1: data to assess the risk of W-1 to aquatic invertebrates.
10. Photodegradate W-1: data to assess the risk of W-1 to fish.
11. Photodegradate B-3: data to assess the risk of B-3 to aquatic invertebrates.
12. PB-7: data to assess the chronic risk of PB-7 to sediment-dwelling organisms.
13. Formulated product: data for an adequate risk assessment for bees. Alternatively, the notifier may include a phrase on the label stating that application is only allowed in greenhouses equipped with insect mesh and in which bees are not used as pollinators, whilst treatment in the field should not be made on flowering crops, and spraying of flowering weeds must be avoided.
14. Formulated product: data for refinement of the long-term risk assessment for earthworms.
15. PB-7: data for the long-term risk assessment for earthworms.
16. PB-4 and PB-22: data for the long-term risk assessment to earthworms.