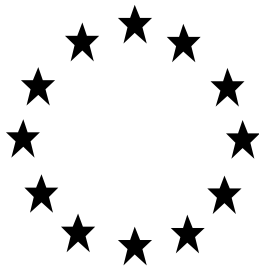
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Folpet

Product type PT 7

(Film preservatives)

Italy

October 2014

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1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

This assessment report has been established as a result of the evaluation of the active substance folpet as product-type PT 7 (film preservatives), carried out in the context of the work programme for the review of existing active substances provided for in Article 89 of Regulation (EU) No 528/2012, with a view to the possible approval of this substance.

Folpet (CAS no. 133-07-3) was notified as an existing active substance, by Makhteshim Agan International Co-ordination Center (MAICC Brussels), hereafter referred to as the applicant, in product-type PT 9.

Commission Regulation (EC) No 1451/2007 of 4 December 2007[1] lays down the detailed rules for the evaluation of dossiers and for the decision-making process.

In accordance with the provisions of Article 7(1) of that Regulation, Italy was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for folpet as an active substance in Product Type PT 9 was [date], in accordance with Annex V of Regulation (EC) No 1451/2007.

On 13 July 2009, Italian competent authorities acting for Italy as the Rapporteur Member State (RMS) received a dossier from the applicant. The RMS accepted the dossier as complete for the purpose of the evaluation on 2010.

On June 2011, the RMS submitted to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report (CAR).

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Agency. Revisions agreed upon were presented at the Biocidal Products Committee and its Working Groups meetings and the competent authority report was amended accordingly.

1.2. Purpose of the assessment report

The aim of the assessment report is to support the opinion of the Biocidal Products Committee and a decision on the approval of folpet for product-type PT 7, and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available from the Agency web-site shall be taken into account.

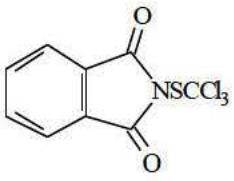
[1] Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

However, where conclusions of this assessment report are based on data protected under the provisions of Regulation (EU) No 528/2012, such conclusions may not be used to the benefit of another applicant, unless access to these data for that purpose has been granted to that applicant.

2. OVERALL SUMMARY AND CONCLUSIONS

2.1.Presentation of the Active Substance

2.1.1. Identity, Physico-Chemical Properties & Methods of Analysis

CAS-No.	133-07-3
EINECS-No.	205-088-6 (Annex I index number: 613-045-00-1)
Other No. (CIPAC, ELINCS)	CIPAC 75
IUPAC Name	N-(trichloromethylthio) phthalimide N-(trichloromethanesulfenyl)phthalimide
Common name, synonym	Folpet
Molecular formula	C9H4Cl3NO2S
Structural formula	

Pure folpet is a white crystalline solid with a reported melting point of 179 - 180 °C. At 20 °C, the vapour pressure of the pure compound is very low. Its solubility in water is 0.8 mg/L at room temperature and it is slightly soluble in a range of organic solvents, particularly those of moderate polarity. It has a medium range octanol/water partition coefficient. Folpet is non-flammable, non-explosive and is not an oxidising agent. In the dry state, it is stable at room temperature, but it is hydrolysed in an aqueous solution at a rate that depends on the pH. In alkaline solution, this breakdown is rapid, occurring within minutes. The hydrolysis products are carbon dioxide, hydrochloric acid, hydrogen sulphide, phthalamic acid, and phthalic acid.

Adequate methodology exists for the determination of the active substance in the technical active substance and in soil, water and air. Analytical methods are provided for water which include determination of metabolites because the targeted analyte (folpet) does not exist in water.

[redacted] is an impurity present in technical folpet at between [redacted] w/w. It is proposed that [redacted] undergoes similar metabolic processes to folpet. In the rat, absorbed folpet is converted to phthalamic acid via phthalimide by the loss of the trichloromethylthio moiety. [redacted] and a trichloromethyldithio moiety. As in the case of folpet, it is expected that the [redacted] that is initially formed undergoes hydrolytic attack resulting in [redacted].
The trichloromethyldithio moiety is most likely to form a conjugate to with GSH, which will undergo the same excretory process as the thiophosgene-GSH conjugate formed from the parent folpet. It is also possible that the [redacted] since the metabolic pathway is expected to be very similar to folpet, the toxicity is also expected to

be very similar. [redacted]

Test substances used in the toxicology and ecotoxicology tests cover the reference specification.

2.1.2. Intended Uses and Efficacy

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against the target organism(s) and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

Folpet is used as a film preservative (PT 7) for use in products including paints, mastics, sealants, fillers and adhesives showing a preservative effect (e.g. wallpaper paste). Products containing folpet may be used by professionals (decorators and builders) and non-professionals. Typical application is manual (by brush, roller or spray apparatus).

In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, , the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.3. Classification and Labelling

The current classification and labelling for folpet according to Regulation (EC) No 1272/2008 is as follows:

Classification according to Directive 67/548/EEC		
Hazard(s)	Xn N	Harmful Dangerous for the environment
Risk Phrase(s)	R20 R36 R40 R43 R50	Harmful by inhalation Irritating to eyes Limited evidence of a carcinogenic effect May cause sensitisation by skin contact Very toxic to aquatic organisms
Safety Phrase(s)	S2 S36/37 S46 S61	Keep out of the reach of children Wear suitable protective clothing and gloves If swallowed, seek medical advice immediately and show the container or label Avoid release into the environment. Refer to special instructions/Safety data sheets
Classification according to Regulation (EC) No 1272/2008		
Hazard Statement Codes	GHS07 GHS08 GHS09	
Hazard Class, category code and Hazard statement	Acute Tox. 4 Eye Irrit. 2 Skin Sens 1 Carc. 2 Aquatic Acute 1	H332: Harmful if inhaled H319: Causes serious eye irritation H317: May cause an allergic skin reaction H351: Suspected of causing cancer H400: Very toxic to aquatic life. M factor 10.

On the basis of information presented in the dossier, it is proposed not to change the current classification and labelling.

2.2.Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification

Folpet technical was of low toxicity by the oral and dermal routes, but was harmful by inhalation and is classified as R20. Folpet was toxic by the intraperitoneal route, however this is not a relevant route of exposure for PT7. Folpet technical was non-irritant to the skin in a guideline, single application study. However, at high doses in a multiple application study irritation was seen. Moderate ocular irritation occurred when applied to the eye, but signs persisted in some animals to termination, and the material is classified as (R36) 'Irritating to eyes'. In a guinea pig maximisation test folpet technical caused positive delayed sensitivity and is classified as (R43) 'May cause sensitisation by skin contact'.

The dramatic decrease in toxicity of oral versus intraperitoneal doses demonstrates that the skin and GI tract are effective barriers to absorption.

Summary of acute toxicity studies with folpet

Study	**Species**	**Results**	**Classification Directive 67/548/EEC**	**Classification Regulation (EC) No 1272/2008**	**Reference**
Acute oral toxicity	Rat	LD50 > 2000 mg/kg bw	-	-	[redacted] (1992a)
Acute dermal toxicity	Rabbit	LD50 > 2000 mg/kg bw	-	-	[redacted] (1982)
	Rat	LD50 >2000 mg/kg	-	-	[redacted] (1991)
Acute inhalation toxicity	Rat	LC50 =1.89 mg/l	R20	Acute Tox. 4	[redacted] (1993)
Acute skin irritation	Rabbit	Non-irritant	-	-	[redacted] (1993)
Acute eye irritation	Rabbit	Moderate irritant	R36	Eye Irrit. 2	[redacted] (1992b)
Skin sensitisation (Magnusson & Kligman)	Guinea pig	Positive	R43	Skin Sens 1	[redacted] (1993)
Acute intraperitoneal toxicity	Rat	LD50 =36-40 mg/kg bw	-	-	[redacted] (1981)

The proposed classification is in respect of the biocidal product. Folpet has also been classified as R40 (Cat. 3 carcinogen) according to Directive 67/548/EEC, Carc 2 according to Regulation (EC) No 1272/2008. The active substance folpet is used as an in-can preservative in paint at a maximum in use concentration of 2g/kg (0.2%). The dilution in

the treated article is therefore less than the <1% w/w cut-off specified in Article 3 of Directive 1999/45/EC, such that the classification for harmful, irritant, sensitising and possible carcinogen do not apply to the treated articles.

Folpet is rapidly absorbed, widely distributed and rapidly excreted after oral administration. The most toxicologically significant pathway is the potential to degrade to the highly reactive metabolite thiophosgene. Metabolism by hydrolysis or by reaction with thiols results in the formation of phthalimide, which is further metabolised to phthalamic acid, phthalic acid and phthalic anhydride Comparison of in vivo rat and in vitro rat and human data for Folpan 50 SC and Folpan 80 WDG showed that dermal penetration of the undiluted formulations as supplied was 0.07% and 0.95%, respectively. At an in-use spray concentration of 1.25 g a.s./L, dermal absorption was 6.54% and 9.19% absorption for Folpan 50 SC and Folpan 80 WDG, respectively. At an in-use spray concentration of 7.5 g a.s./L, dermal absorption was 6.24% and 4.22% for Folpan 50 SC and Folpan 80 WDG, respectively. Excretion of absorbed material was rapid and analysis of the material in the skin showed that the absorbed material was predominantly in the form of known metabolites of folpet, with little or no parent material actually absorbed.

In short term studies, rats and mice tolerated oral doses of folpet more readily than the dog with the 90 days NOAEL in the rat being 1000 ppm. A NOAEL for 90 days in the dogs was not established but the 52 weeks NOAEL was 10 mg/kg bw/d. Treatment was associated with reduced bodyweight gain and food consumption at higher dose levels. Treatment was also associated with histopathological changes in the gastrointestinal tract associated with the irritant nature of folpet: hyperkeratosis of the oesophagus, hyperkeratosis and acanthosis in the non-glandular stomach in rats, vomiting and diarrhoea in dogs, with none-specific clinical chemistry findings and organ weight changes associated with reduced body weights. Folpet appeared to be less well tolerated in the rat by dermal administration, principally because of irritation. A LOAEL of 1 mg/kg bw/d was determined for local effects in a 28-day dermal toxicity study.

In mutagenicity studies, folpet was not mutagenic in vivo, but showed apparent mutagenic activity in certain in vitro assays. Folpet and its analogue captan have been shown to be capable of causing base pair substitution and frame-shift mutations in bacterial reverse mutation assays and mutations in in vitro mammalian forward mutation assays. Cytogenetic changes in mammalian cell lines in vitro were also seen as was DNA damage in bacteria, non-mammalian eukaryotes and in some mammalian cell lines. Mutagenicity was greatly reduced in the presence of S-9 mix, mammalian blood, glutathione or cysteine in bacteria and in mammalian cell lines in vitro, indicating that detoxification occurs with metabolic activation and in intact organisms. Negative results were obtained in in vivo mammalian mutation assays and chromosomal damage assays. This would indicate that in intact organisms there are mechanisms which react with the parent compound thus abolishing its genotoxic activity. Data from mammalian studies with folpet and the closely-related captan support the conclusion that the trichloromethylthio side chain (common to both molecules) is the active part of the molecule and that it is detoxified by glutathione and other endogenous thiols. Captan, and by inference, folpet do not interact directly with DNA in vivo.

Folpet is not carcinogenic in the rat at levels up to 5000 ppm. Folpet is carcinogenic in mice at levels of 1000 ppm and greater; high dose levels were associated with increased incidence of carcinoma in the duodenum, and hyperkeratosis of the skin, oesophagus and stomach, hyperplasia of the duodenum, hyperplasia of the jejunum and dose-related neoplasms in the duodenum, stomach and jejunum. These data are consistent with the nature of folpet's interaction in the mammal i.e. folpet is an irritant. In the mouse this irritation causes changes to the architecture of the gastro-intestinal tract that are associated with the eventual tumour development. In the rat, irritation is seen primarily in the upper gastro-intestinal tract (e.g. oesophagus and non-glandular stomach), but these changes are not associated with tumour enhancement. As tumours are produced via an irritation mechanism, the appropriate risk assessment involves a margin of exposure evaluation (i.e. a threshold phenomenon).

Folpet is not teratogenic to the rat or rabbit. No effects on reproductive parameters, fertility or presence of foetal malformations were evident in two multi-generation studies in the rat. Treatment was associated with reduced bodyweight gain in adults and offspring, and reduced food consumption in adults. Histopathology revealed hyperkeratosis of the non-glandular stomach consistent with findings in short-term studies in rats.

Classification of folpet for reproductive toxicity (pre-natal developmental toxicity) has previously been considered plant protection products approval and harmonised classification and labelling process. Folpet C&L is included in Annex VI to CLP Regulation. No new data are available, therefore no change in classification is proposed.

Folpet is a film preservative used in various products including paints, mastic, sealants, fillers and adhesives. Therefore, any exposure of the end user arising from this usage pattern is to the active substance folpet.

2.2.1.2. Effects assessment

A long-term (chronic) AEL of 0.1 mg/kg bw/d is derived for folpet based on the NOAEL of 10 mg/kg bw/d from the 1-year dog study and supported by the 2-year rat study. A standard assessment factor of 100 is considered to be appropriate. Correction for the extent of gastrointestinal absorption is not required.

A medium-term AEL of 0.1 mg/kg bw/d is derived for folpet based on the maternal NOAEL of 10 mg/kg bw/d from the rabbit developmental toxicity study. A standard assessment factor of 100 is considered to be appropriate. Correction for the extent of gastrointestinal absorption is not required.

An acute AEL of 0.2 mg/kg bw/d is derived for folpet based on the developmental NOAEL of 20 mg/kg bw/d from the rabbit developmental toxicity study. A standard assessment factor of 100 is considered to be appropriate. Correction for the extent of gastrointestinal absorption is not required.

Folpet: proposed AEL values

AEL	**Value**	**Study**	**Endpoint**	**Assessment factor**
Chronic AEL	0.1 mg/kg bw/d	1-year dog 2-year rat	10 mg/kg bw/d	100
Medium-term AEL	0.1 mg/kg bw/d	Rabbit developmental toxicity	10 mg/kg bw/d (maternal NOAEL)	100
Acute AEL	0.2 mg/kg bw/d	Rabbit developmental toxicity	20 mg/kg bw/d (developmental NOAEL)	100

While folpet is not classified as a skin irritant based on the results of a skin irritation study, Folpet is classified as skin sensitiser Cat 1 according to CLP Regulation (Reg. (EC) n. 1272/2008). The levels of folpet achieved in the end-use product of 2 g/kg (0.2 %) are much lower than the concentrations used in the Maximisation study. Considering the CLP sub-categories (Skin Sens. 1A and 1B) , folpet would not be classified as a strong sensitiser based on the results of the maximisation study and is therefore considered to have low to moderate potency as a sensitiser.

2.2.1.3. Exposure assessment

Human exposure assessments have been conducted where EU guidance is available. Assessments have been made in accordance with the Technical Notes for Guidance (TNsG)

for Human Exposure to Biocidal Products, Guidance on Exposure estimation (June 2002 and June 2007) [2]. Exposure assessments are based on default values.

Folpet is used as a preservative in products at a maximum in use concentration of 2 g a.s./kg (0.2%). Products can be used by professional and non-professional users. The uses of folpet as a film preservative, together with relevant assumptions based on EU guidance are summarised in the table below:

	User	Application method	Usage assumptions
Film preservative (PT7)	Professional	Spraying	360 minutes, daily
		Brush and roller	360 minutes/day
	Non-professional	Brush and roller	4 hours/day; 2-5 days per year

Products for application by spray will not be available to non-professionals.

It is assumed that brush/roller cleaning will occur. Suggested values for cleaning are 5 minutes for a hand-washing a paint brush and 10 minutes for a paint roller, where water-based products are used (TNsG for PT7.02).

The potential for exposure to folpet is summarised in the table below and considered in more detail in the subsequent text.

Exposure path	**Industrial use**	**Professional and non professional use**	**General public**	**Via the environment**
Inhalation	Not relevant	Potentially significant	Negligible	Negligible
Dermal	Not relevant	Potentially significant	Negligible	Negligible
Oral	Not relevant	Negligible	Negligible	Negligible

Folpet is not volatile (vapour pressure = 2.1 x 10^{-5} Pa at 25°C), therefore the exposure to vapour will be minimal. However inhalation exposure to folpet in aerosolised product may occur under some application types, such as spray application. Primary oral exposure to folpet is likely to be minimal, therefore the dermal route will be the most important route of exposure.

Professional exposure

The potential exposure of professionals applying biocidal products containing folpet by brush/roller or by spraying, based on default values in EU TNsG document Part 2 June 2002, is assessed below. This exposure scenarios used are a representation of a realistic worst-case situation.

The following points have been taken into consideration:

[2] Technical Notes for Guidance (TNsG) for Human Exposure to Biocidal Products, Guidance on Exposure estimation (final June 2002), European Commission, DG Environment, Ref: B4-3040/2000/291079/MAR/E2.
Technical Notes for Guidance (TNsG) for Human Exposure to Biocidal Products, (June 2007). Document endorsed at the 25th meeting of representatives of Members States Competent Authorities for the implementation of Directive 98/8/EC concerning the placing of biocidal products on the market (19-21 June 2007).

1. It is assumed that 100% of dermal exposure is absorbed through clothing.
2. If PPE is needed, gloves will reduce exposure of hands by 90% (EU Guidance Document Section 2.3 of Part 2, June 2002). Protective impermeable coveralls are assumed to reduce exposure of the whole body (excluding hands) by 95%.
3. It is assumed that 100% of inhalation exposure is absorbed. For dermal absorption of the active substance folpet a value of 10% is used (to be consistent with the EU review of folpet as a plant protection product under Directive 91/414/EEC).
4. Operator body weight (professional users) is assumed to be 60 kg.

Professional users are fully trained as part of their job and handle such end use products on a day to day basis.

Results of assessment

Exposure assessment of professional operators using products containing to folpet at a concentration of 2 g a.s./kg:

- Brush and roller application (with and without gloves scenario), based upon the highest data for hand exposure (uncertainty is high) and on the 75th percentile for body exposure and inhalation exposure (uncertainty is moderate).
- Paint spraying (with gloves only and with gloves + coverall scenario), based upon 75th percentile for hand, body and inhalation exposure (uncertainty is moderate).

Total systemic exposure is shown in the table below.

Scenario	**Systemic exposure (mg/kg bw/d)**
	Folpet
Brush and roller application (no gloves):	**0.224**
Brush and roller application (gloves):	**0.062**
Paint spraying (no gloves)	**0.54**
Paint spraying (gloves; no RPE)	**0.3**
Paint spraying (gloves + coverall; no RPE)	**0.0218**
Brush washing (no gloves)	**0.00057**
Cleaning of spray equipment (no gloves)	**0.0000072**

Non-professional exposure

The assessment to non-professional users is based on EU default values.

Products for application by spray will not be available to non-professionals.

The potential exposure of non-professional users applying biocidal products containing folpet by brush/roller, based on default values in EU TNsG document Part 2 June 2002, is assessed below. This exposure scenarios used are a representation of a realistic worst-case

situation.

The following points have been taken into consideration:

1. It is assumed that 100% of dermal exposure is absorbed through clothing.
2. It is assumed that 100% of inhalation exposure is absorbed. For dermal absorption of the active substance folpet a value of 10% is used (to be consistent with the EU review of folpet under Directive 91/414)
3. Operator body weight (average for non-professional male and female users) is assumed to be 60 kg.

Operator body weight is assumed to be 60 kg (average for non-professional male and female users).

Results of assessment

Total systemic exposure to folpet of non-professional operators using products containing the active substance at a concentration 2 mg a.s./kg without gloves based upon the highest data for hand exposure (uncertainty is high) and on the 75th percentile for body exposure and inhalation exposure (uncertainty is moderate), is shown in the table below.

Scenario	**Systemic exposure** (mg/kg bw/d)
	Folpet
Brush and roller application (no gloves):	***0.15***

Secondary exposure

Indirect exposure to non-users is assumed to be negligible, however the potential for exposure resulting from a number of worst-case scenarios are considered below:

Exposure scenario	**Systemic exposure** (mg/kg bw)
	folpet
Laundering contaminated overalls (acute)	***0.016***
Dermal contact with wet product by child (acute)	***0.17***
Oral ingestion child (acute)	***0.041***
Inhalation exposure child (acute)	***0.0008***
Dermal contact with surface bloom on preserved mastic (acute)	***0.025***

2.2.1.4. Risk characterisation

Professional use

The potential exposure of professional users during use of paints, mastic, sealants, fillers or adhesives containing the preservative folpet is assessed and summarised in the table below.

Use scenario	Systemic exposure to folpet	
	(mg/kg bw/d)	**% AEL***
Brush and roller application (no gloves):	0.224	240
Brush and roller application (with gloves):	0.062	62
Paint spraying (no gloves)	0.54	540
Paint spraying (gloves only)	0.3	300
Paint spraying (gloves + coverall no RPE)	0.0218	22
Paste application	Likely to be acceptable	<100

**Folpet medium-term AEL= 0.1 mg/kg bw/d*

Considering professional users working 360 min each day for brush and roller application and 360 min/day for spray application, with no gloves, worst-case default exposure values on a daily basis achieved 224% and 540 of the AEL respectively, respectively; however it has to be underlined that, for professional users[3], in the case of products that are sensitizers and/or irritants (Folpet is classified as R 43: may cause sensitization by skin contact) the actual exposure data has to be used with the provision that users will have to wear gloves.

If exposure estimates were based on more realistic values (considering gloves and coverall) the exposure would be correspondingly lower resulting in lower risk to professional workers. The exposure is based on daily working rates and therefore the combination of any individual tasks is not applicable.
In conclusion, exposure levels resulting from the intended professional uses of products containing the film preservative folpet on a daily basis are therefore estimated to be below the AEL when PPE such as gloves and coverall are worn.

Folpet is not classified as a skin irritant based on the results of a skin irritation study, according to CLH Folpet is classified as skin sensitiser Cat 1. The levels of folpet achieved in the end-use product of 2 g/kg (0.2 %) are below the threshold for classification of the product according to Directive 99/45/EEC

Risk characterisation: professional uses

Exposure Scenario	**PPE**	**Estimated systemic exposure (mg/kg bw/d folpet)**	**Relevant NOAEL (mg/kg bw/d)**	**MOE**	**% AEL**
Brush and roller application (Painting Model 1)	None	0.224	10	45	224
	Gloves	0.062		89	112

[3] Professional users have access to Material Safety Data Sheets (MSDS) and may have some basic knowledge about classification and labeling. The workers are trained and skilled in the main objectives of their occupation and may have some experience and skill in the use of personal protective equipment (PPE) if that is necessary for their normal work

Brush/roller (PHED)	None	0.014		714	14
	Gloves	0.002		5000	2
Brush washing	None	0.00057		17544	0.6
	Gloves	0.00006		1666666	0.06
Paint spraying	None	0.54		18	540
	Gloves	0.3		33	300
	Gloves & coverall	0.0218		459	22
Airless spraying (PHED)	None	0.0005		20000	0.5
	Gloves	0.0004		25000	0.4
Cleaning spray equipment	None	0.0000072		1388889	0.007

Exposure Scenario	**PPE**	**Estimated systemic exposure (mg/kg bw/d folpet)**	**Relevant NOAEL (mg/kg bw/d)**	**MOE**	**% AEL Acute***
Brush and roller application (Painting Model 1)	None	0.224	20	90	112
	Gloves	0.062		322	31
Brush/roller (PHED)	None	0.014		1429	7
	Gloves	0.002		10000	1
Brush washing	None	0.00057		35087	0.3
	Gloves	0.00003		66667	0.02
	None	0.54		37	270
Paint spraying	Gloves	0.3		67	150
	Gloves & coverall	0.0218		917	11
Airless spraying (PHED)	None	0.0005		40000	0.3
	Gloves	0.0004		50000	0.2
Cleaning spray equipment	None	0.0000072		2777778	0.004

** Folpet acute AEL = 0.2 mg/kg bw/d*

Non-professional use

The potential exposure of non-professional users during use of products containing the preservative folpet is assessed and summarised in the table below.

Use scenario	Systemic exposure to folpet	
	(mg/kg bw/d)	**% AEL***
Brush and roller application (no gloves):	***0.074***	75

**the acute AEL for folpet is 0.2 mg/kg bw/d*

The intended uses for non-professional users during use of paint containing the preservative folpet on a daily basis are below the AEL when based on worst-case default values. The exposure assessment has been conducted considering non professional uses working 4 hours each day, with no gloves[4], and 100% dermal exposure through clothing. Based on these assumptions and worst-case default exposure values the exposure estimate is 150% the AEL. Considering the exposure assessment the use of paint containing the preservative folpet for non professionals is not supported.

Risk characterisation: non-professional uses

Exposure Scenario	PPE	Estimated systemic exposure (mg/kg bw/d folpet)	Relevant NOAEL (mg/kg bw/d)	MOE	% AEL*
Brush and roller application	None	0.15	20	133	75

* *Folpet acute AEL =0.2 mg/kg bw/d*

Indirect exposure as a result of use

Potential indirect exposure is most likely to occur via inhalation of volatile components from freshly painted surfaces following use. However, the inhalation risk to users (professional and non-professional) without any respiratory protection using the products on a day to day basis is minimal. Therefore, it is considered that any incidental exposure to non-users will be of a lesser concern.

The most likely route of indirect exposure may be either via washing of contaminated overalls or via dermal contact with wet paint (see Section IIB 3.2.4)

Since the two scenarios considered for secondary exposure (e.g.: Laundering contaminated overalls and Dermal contact with wet product by child) are both acute scenarios, the acute AEL of 0.2 mg/kg bw should be used as an appropriate endpoint. The acute AEL is appropriate for use as reference value for the protection of the sensitive sub-population (i.e. pregnant mothers). The value represents a conservative/protective position of a small child of 15kg and as such therefore represents a worst-case.

[4] Non-professional users are usually consumers - who may or may not read a product label. There is an expectation - but little guarantee - that non-professionals will comply with instructions for use of a product. They have no access to controls or formal PPE, though they may use household protective equipment.

Exposure scenario	Systemic exposure	
	(mg/kg bw)	**% AEL ***
Laundering contaminated overalls	0.016	8
Dermal contact with wet product by child	0.17	85
Oral ingestion child	0.041	20
Inhalation exposure child	0.0008	0.4
Dermal contact with surface bloom on preserved mastic	0.025	12.5

** the acute AEL for folpet is 0.2 mg/kg bw*

Indirect acute exposure levels resulting from the intended use of folpet as a film preservative are therefore estimated to be below the acute AEL when based on worst-case default values.

Risk characterisation: secondary exposure

Exposure Scenario	**Estimated systemic exposure (mg/kg bw/d folpet)**	**Relevant NOAEL (mg/kg bw/d)**	**MOE**	**% Acute AEL**
Laundering contaminated overalls	0.016	**20**	**1250**	**8**
Dermal contact with wet product by child	0.17		**118**	**85**
Oral ingestion child	0.041		**488**	**21**
Inhalation exposure child	0.0008		**25000**	**0.4**
Dermal contact with surface bloom on preserved mastic	0.025		**800**	**12.5**

Combined exposure

Professional and non-professional users are potentially at risk of exposure from several sources during or after use of products containing folpet. The following combined exposure scenarios for professional and non professional uses are taken into consideration:

- Professional uses
  - Brush and roller application exposure and brush washing

- Spray application and cleaning spray equipment
- Non professional uses
  - Brush and roller application exposure and brush washing

Exposure scenario	Estimated systemic exposure (mg/kg bw/d folpet)	Combined estimated exposure (mg/kg bw/d folpet)	Relevant NOAEL (mg/kg bw/d)	MOE	% AEL*
Brush and roller application	0.062[1]	0.0625	10	160	63
Brush washing	0.00057				
Spray application	0.0218[2]	0.0218	10	459	22
Cleaning spray equipment	0.0000072				

[*] *Folpet medium-term AEL =0.1 mg/kg bw/d*
[1] *with the use of gloves*
[2] *with the use of impermeable coveralls and gloves*

Exposure scenario	Estimated systemic exposure (mg/kg bw/d folpet)	Combined estimated exposure (mg/kg bw/d folpet)	Relevant NOAEL (mg/kg bw/d)	MOE	% AEL*
Non professional uses					
Brush and roller application	0.15	0.1505	20	133	75

Folpet acute AEL =0.2 mg/kg bw/d

Based on the calculations the combined exposure to paints containing folpet following brush and roller application, and brush washing, as well as, spray application and cleaning spry equipment, lead to exposure levels below the AEL.

Local dermal risk assessment

Folpet is not a skin irritant, but is classified as a sensitiser. The skin sensitisation study (Maximisation design) performed with folpet (Rees, 1993b) used an intradermal induction concentration of 10%. The study showed a 100% positive response following challenge with a concentration of 50% folpet and a 75% response following challenge with 10% folpet. The levels of folpet achieved in the end-use product of 2 g/kg (0.2 %) are much lower than the concentrations eliciting positive responses in this study. Additionally, the concentrations of folpet are below the threshold for classification of the product according to Directive 99/45/EEC.

While folpet is not classified as a skin irritant based on the results of a skin irritation study, repeated dermal application in a 28-day study resulted in significant local effects in all groups (0.5 mg/ml; 1 mg/kg bw/d and above). The findings of this study, in which folpet was repeatedly applied for 6 hour periods in mineral oil under occlusive conditions are not considered to be of direct relevance to the human risk assessment. Ready-to-use products

(PT6, PT7) typically contain folpet at levels of 0.2%; risk assessment for professional workers requires the use of gloves. It is therefore considered very unlikely that the normal use of folpet products would result in a level of dermal contamination resulting in local irritation. Moreover, all studies had been evaluated according to CLP and no classification is required.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Ready biodegradation

In a ready biodegradability test folpet was applied to the inoculum at 1.0 mg/L, *i.e.* at approximately the solubility limit. Under these conditions, there was a lag phase of ca 4 days, but the plateau – signifying substrate exhaustion – was effectively reached by day 19. CO_2 production reached 60% within 28 days and within 10 days of crossing the 10% threshold. When the physical constraints of bioavailability to the inoculum are removed, (i.e. when exposure is at environmentally relevant concentrations) folpet meets the criteria for classification as readily biodegradable fulfilling the 10 day window criteria.

Biodegradation in aquatic systems

The behaviour of folpet in the aquatic environment was investigated in two dissimilar water/sediment systems (silty clay and sandy loam) in a study conducted at 20°C to SETAC 1995/BBA Part IV, 5-1 guidelines. In each test, folpet was rapidly degraded in both the overlying water and the whole system, with DT_{50} values of 0.014 to 0.018 days (equating to a worst-case value of 0.4 hours). The equivalent range of degradation rates at the EU average temperature of 12°C can be estimated to be 0.03 to 0.04 days.

Folpet was metabolised to carbon dioxide (51 to 54% AR after 100 days) as a principal metabolite. Low recoveries (<90% AR) were obtained at most sampling intervals, partly due to the loss of carbon dioxide during sample processing. Reference to the production of methane from the anaerobic biodegradation of phthalates is reported in the literature[5] and it is considered that such metabolism had taken place in the anaerobic sediment layer. As the rate of carbon dioxide production was steady throughout the study, it is thought likely that the rate of methane production was also steady throughout the study and the reason for the low mass balance. The study is acceptable because degradation of folpet is very fast in the study (<1d) and the low mass balances were observed after 1 day.

The major metabolites (>10% AR) recovered from the water phase were phthalimide (max. 20.4 to 26.0% AR at 4 h), phthalamic acid (max. 13.3% AR at 1h), phthalic acid (max. 26.3 to 37.5% AR at 1d), benzamide (max. 10.2% AR at 1 d) and 2-cyanobenzoic acid (max. 39.7% AR at 1d). These metabolites were all readily degraded in the surface water phase and the whole system.

A summary of the degradation rates is provided in the following table. The estimated degradation rates at 12°C are also shown.

[5] Shelton, D. R., Boyd, S. A., and Tiede, J. M. (1984). Anaerobic biodegradation of phthalic acid esters in sludge. Environmental Science and Technology, 18, 93-97.

Degradation rate (DT_{50}) for the major metabolites of folpet in water/sediment systems

Compound	Medium	DT_{50} (days) at 20°C	DT_{50} (days) at 12°C
Phthalimide	Silty clay aqueous phase	0.54	1.15
	Silty clay total sediment/water	0.58	1.23
	Sandy loam aqueous phase	0.59	1.25
	Sandy loam total sediment/water	0.65	1.38
Phthalamic acid	Silty clay aqueous phase	3.55	7.54
	Silty clay total sediment/water	3.98	8.46
	Sandy loam aqueous phase	5.50	11.69
	Sandy loam total sediment/water	6.09	12.94
Phthalic acid	Silty clay aqueous phase	1.38	2.93
	Silty clay total sediment/water	1.41	3.00
	Sandy loam aqueous phase	6.36	13.51
	Sandy loam total sediment/water	6.45	13.70
Benzamide	Silty clay aqueous phase	1.63	3.46
	Silty clay total sediment/water	1.63	3.46
	Sandy loam aqueous phase	[a]	[a]
	Sandy loam total sediment/water	[a]	[a]
2-Cyanobenzoic acid	Silty clay aqueous phase	0.33	0.70
	Silty clay total sediment/water	0.36	0.76
	Sandy loam aqueous phase	0.67	1.42
	Sandy loam total sediment/water	0.72	1.53

[a] Insufficient data for analysis.

The main metabolites encountered in the sediment were phthalimide (max. 5.9% AR) and phthalic acid (max. 3.8% AR). Sediment unextracted residues increased to *ca* 25% AR between day 7 and day 14 but were declining at the end of the study at 100 days. Unextracted residues were shown to be mainly associated with the humin fraction, probably due to phthalate formation. The decline of unextracted residues is most probably due to anaerobic degradation of the bound phthalates resulting in methane production (not collected in the study resulting in low mass balance).

Overall, folpet is not considered to be persistent in the aquatic environment.

Exposure of the aquatic environment following the biocide use of folpet under PT7 will be predominantly via disposal/run-off to drain and processing through STP. Under these circumstances the possibility of folpet entering natural waters and sediment is extremely remote.

Biodegradation in Soil

Folpet, is rapidly degraded in a range of aerobic soil types at temperatures of 20 and 25°C under laboratory conditions, with first-order DT_{50} values in the range of 0.2 to 4.3 days. The degradation of folpet under aerobic conditions at a lower temperature of 10°C was measured to be 3.8 days in a silt loam soil (corresponding value at 20°C was 0.8 days). The equivalent range of soil degradation rates at the EU average temperature of 12°C can

be estimated to be 0.4 to 14.3 days. However, the data suggest that factors other than temperature (e.g. soil pH) have a significant influence on soil degradation. Levels of bound residues initially accumulated to a level of 31.2% AR at day 14, but subsequently declined resulting in substantial mineralisation to CO_2. (up to 60% AR after 90 days).

Overall, folpet is not considered to be persistent in soil.

The compounds phthalimide (max 65% AR after 5 days), phthalamic acid (max 16.7% AR after 1 day) and phthalic acid (max 16.6% AR after 1 day) are the major (>10% AR) degradation products of folpet in soil. These compounds are also rapidly degraded in soil with DT_{50} values in the range of 0.5 to 4.8 days, 0.4 days and 0.6 to 4.1 days, respectively at 20°C. The equivalent range of soil degradation rates at the EU average temperature of 12°C can be estimated to be 1 to 10 days, 0.9 days and 1.3 to 8.7 days, respectively.

Overall, phthalimide, phthalamic acid and phthalic acid are not considered to be persistent in soil.

The environmental fate and distribution of folpet has previously been reviewed at EU level under Directive 91/414/EEC, with Italy as the RMS. Conclusions of this review are published in the EFSA Scientific Report (2009) 297, 1-80 (Conclusion on the Peer Review of Folpet) and the following FOCUS normalised degradation rates for folpet, phthalimide and phthalic acid in soil were agreed and have been used in the modelling of environmental exposure for PT7:

Folpet DT_{50} (20°C) = 4.68 days (mean value concluded in the EFSA scientific report)[6].
Phthalimide DT_{50} (20°C) = 7.88 days (mean value concluded in the EFSA scientific report).
Phthalic acid DT_{50} (20°C) = 1.37 days (mean value concluded in the EFSA scientific report).

A study investigating degradation of folpet under anaerobic conditions was performed using US EPA guidelines and involved initial incubation under aerobic conditions (4 days) following by flooding and incubation under anaerobic conditions for a further 60 days. Under these conditions, the degradation of folpet in the soil layer was slower compared to fully aerobic conditions, with a maximum DT_{50} value of 13.5 days. Degradation resulted in the metabolites phthalimide (max 50.6% AR at the start of the anaerobic phase of the study) and phthalic acid (max 13.3% after 60 days of the anaerobic phase). The DT_{50} value for the degradation of phthalimide in the soil layer, under anaerobic conditions, was estimated to be 33.6 days. A second study (supporting information) was conducted which exposed soil to anaerobic conditions for 365 days. Folpet had completely degraded in this study at the time of the initial sampling (7 days) and levels of phthalic acid/phthalamic acid (not chromatographically separated) reached 44.6% AR after 112 days. A metabolite not observed under aerobic conditions, 2-cyanobenzoic acid, was also present at low levels (maximum 5.7% AR). Substantial mineralisation to carbon dioxide was observed in both studies (maximum 26.3% AR after 60 days in the US EPA study and 78.8% after 365 days in the supporting study). CO_2 evolution was not as rapid as compared to fully aerobic conditions.

No laboratory degradation studies have been carried out using a labelled thiophosgene moiety of folpet, however an estimate of the behaviour of this moiety may be made from studies on the closely related compound, captan, which has an identical side chain. These studies, which are discussed and concluded in the EFSA Scientific Report (2009) for Folpet, indicate that the thiophosgene side-chain is likely to be degraded rapidly, resulting in extensive mineralisation to carbon dioxide (up to 80 to 91% AR after 28 to 30 days). Thiophosgene is expected to be unstable because of rapid hydrolysis to thiocarbonic acid and the EFSA expert conclusion was that free thiophosgene will not reach significant levels in soil. This conclusion is considered more robust for the biocidal use of folpet since soil exposure will always be via a secondary route (STP) and residues of folpet in soil are not expected under actual conditions of use.

Soil photolysis of folpet was studied in a sandy loam soil type at 25°C, using both natural and artificial sunlight sources. In the soil samples exposed to natural sunlight and those irradiated

[6] The correct DT_{50} value is the geometric mean = 1.3 days at 20°C. The equivalent DT_{50} at 12°C = 2.47 days using TGD equation 25. The EFSA agreed endpoint represents a worst-case value and has been used in the risk assessment.

with an artificial light source, the degradation observed in the dark controls was comparable to that of the exposed samples. In dark control and irradiated samples, phthalimide was the principle degradation product (maximum 43.6% AR after 31 days for natural sunlight irradiation and maximum 40.0% AR after 31 days in the corresponding dark control). The results indicate that photodegradation is not a significant route of degradation for folpet.

Field soil dissipation data show that degradation of folpet and phthalimide is rapid with the DT_{50} estimated to be less than 3 days for each substance. Highest residues were detected in the 0-15 cm soil horizon, with little or no movement to lower soil horizons. The field dissipation data confirms the results obtained from laboratory tests and shows that folpet and phthalimide (the principle soil metabolite) do not accumulate in soil.

A summary of the soil degradation data is shown in the following tables.

Summary of aerobic laboratory soil degradation rates of folpet and major metabolites

Component	DT_{50} (days)	DT_{90} (days)	Method of calculation	Soil Properties
Folpet	2	7[a]	25°C Not stated.	US Sandy Loam pH = 6.8, OC = 1.03%
	4.3	14[a]	25°C 1st order kinetics, r^2 = 0.97	US Sandy Loam pH = 5.4, OC = 1.16%
	3.8	12.8	20°C 1st order kinetics, r^2 = 0.995	UK Loamy Sand pH = 4.8, OC = 0.9%
	0.8	2.8	20°C 1st order kinetics, r^2 = 0.986	UK Silty Loam pH = 6.2, OC = 2.6%
	0.2	0.7	20°C 1st order kinetics, r^2 = 0.999	UK Clay Loam pH = 7.5, OC = 3.9%
	3.8	12.6	10°C 1st order kinetics, r^2 = 0.998	UK Silty Loam pH = 6.2, OC = 2.6%
Phthalimide	Minor metabolite		25°C	US Sandy Loam pH = 6.8, OC = 1.03%
	7.84	40.02	25°C √1st order kinetics, r^2 = 0.76	US Sandy Loam pH = 5.4, OC = 1.16%
	4.8	16.1	20°C 1st order kinetics, r^2 = 0.876	UK Loamy Sand pH = 4.8, OC = 0.9%
	1.7	5.8	20°C 1st order kinetics, r^2 = 0.992	UK Silty Loam pH = 6.2, OC = 2.6%
	0.5	1.7	20°C 1st order kinetics, r^2 = 0.984	UK Clay Loam pH = 7.5, OC = 3.9%
	3.2	10.6	10°C 1st order kinetics, r^2 = 0.977	UK Silty Loam pH = 6.2, OC = 2.6%

Component	DT_{50} (days)	DT_{90} (days)	Method of calculation	Soil Properties
Phthalic acid	Minor metabolite		25°C	US Sandy Loam pH = 6.8, OC = 1.03%
	Minor metabolite		25°C	US Sandy Loam pH = 5.4, OC = 1.16%
	4.1	13.7	20°C 1st order kinetics, r^2 = 0.892	UK Loamy Sand pH = 4.8, OC = 0.9%
	1.0	3.2	20°C 1st order kinetics, r^2 = 0.954	UK Silty Loam pH = 6.2, OC = 2.6%
	0.6	2.1	20°C 1st order kinetics, r^2 = 0.999	UK Clay Loam pH = 7.5, OC = 3.9%
	1.8	5.9	10°C 1st order kinetics, r^2 = 0.855	UK Silty Loam pH = 6.2, OC = 2.6%
Phthalamic acid	Minor metabolite		25°C	US Sandy Loam pH = 6.8, OC = 1.03%
	0.4	1.3	20°C 1st order kinetics, r^2 = 0.999	UK Silty Loam pH = 6.2, OC = 2.6%
	0.8	2.7	10°C 1st order kinetics, r^2 = 0.973	UK Silty Loam pH = 6.2, OC = 2.6%

a Estimated visually.

Summary of anaerobic laboratory soil degradation rates of folpet and major metabolites

Component	DT_{50} (days)	DT_{90} (days)	Method of calculation	Soil Properties
Folpet	14.6	48.5[a]	25°C 1st order kinetics, r^2 = 0.980 anaerobic whole system	US Sandy Loam pH = 5.4, OC = 1.16%
	13.5[a]	65[a]	25°C anaerobic soil phase only	US Sandy Loam pH = 5.4, OC = 1.16%
Phthalimide	33.6[a]	110[a]	25°C anaerobic soil phase only	US Sandy Loam pH = 5.4, OC = 1.16%
Phthalic acid	Minor metabolite		25°C	US Sandy Loam pH = 5.4, OC = 1.16%
Phthalamic acid	Minor metabolite		25°C	US Sandy Loam pH = 5.4, OC = 1.16%

a Extrapolated from the study data by the applicant.

Hydrolysis

Folpet hydrolyses rapidly in sterile water and the rate of hydrolysis increases rapidly with pH.

Hydrolysis half-life data for folpet was measured at a temperature of 25°C, at pH5, pH7 and pH9 under sterile conditions and the measured rates were: 2.6 hours at pH5 1.1 hours at pH7 and 0.019 hours at pH9. Hydrolysis half-life data for folpet was also measured at 25°C and 40°C, at pH4, pH7 and pH9 under sterile conditions and the measured rates were: 6.51 hours at pH4 and

25°C, 1.06 hours at pH4 and 40°C, 0.70 hours at pH 7 and 25°C, 0.18 hours at pH 7 and 40°C. At pH9 the rate of reaction was too rapid to measure. The equivalent hydrolysis degradation rates at the EU average temperature of 12°C can be estimated to be: pH4 = 17.1 hours (mean), pH5 = 8.7 hours, pH7 = 2.7 hours (mean) and pH9 = 0.1 hours. At pH 5 the predominant degradate is phthalimide but there is a shift towards phthalic acid which becomes the predominant degradate at pH 9. Kinetic analysis suggested that hydrolysis takes place both from folpet and phthalimide at higher pH values and from folpet only at low pH values. The metabolite phthalimide is also rapidly hydrolysed. The measured rates were: 5.49 hours at pH4/100°C, 7.45 hours at pH7/40°C, 1.99 hours at pH9/25°C and 0.28 hours at pH9/40°C. The equivalent hydrolysis degradation rates at the EU average temperature of 12°C can be estimated to be: pH4 = 3695 hours, pH7 = 88 hours and pH9 = 5.0 hours (mean).

Hydrolysis is therefore the primary route of degradation for folpet in the aquatic environment.

Photolysis

The instability of folpet towards chemical hydrolysis, even at low pH, means that photolysis is not a significant degradation pathway in the aquatic environment. The results of an aqueous photolysis study, where very similar degradation results are found in the absence or presence of ligh, confirm this conclusion.

Adsorption

The adsorption/desorption coefficient of folpet cannot be reliably estimated by methods, such as the batch equilibrium method, because of rapid degradation in soil and in aqueous media. The lowest estimated adsorption/desorption coefficient is 304 mL/g. The adsorption/desorption coefficient of phthalimide, the major soil metabolite, was estimated in five soils of European origin using the batch equilibrium method. The Koc values determined for phthalimide were in the range 55.7 to 293.1 mL/g. The Koc values for phthalamic acid and phthalic acid were not determined experimentally, however QSAR estimates for these metabolites range from 1.206 to 80.85 L/kg. In addition, the results of an aged soil leaching study with radiolabelled folpet suggest that folpet and its soil degradation products are unlikely to leach significantly through soil, with less than or equal to 0.1% of applied radioactivity found in the leachate.

Bioaccumulation

The logKow of folpet is 3.017. Based on a laboratory study in which bluegill sunfish were exposed to folpet at artificially maintained concentrations, the whole fish BCF was 56, with a subsequent depuration DT_{50} of 0.63 days. The low measured BCF value of folpet indicates a low potential for bioaccumulation, even under worst-case, unrealistic exposure conditions. The environmentally relevant entities that arise from the biocidal uses of folpet are its degradation products rather than the parent active substance. Log Kow estimates obtained using the KOWWIN model in EPISUITE are all lower than that of the parent compound and below the trigger of 3.0. It may therefore be concluded that the breakdown products of folpet also pose negligible potential for bioaccumulation.

Volatilisation

The Henry's Law constant for folpet is 8×10^{-3} $Pa.m^3.mol^{-1}$. Folpet is a solid with a relatively high melting point and low vapour pressure and can therefore be considered as non-volatile. Concentrations in air are expected to be negligible during use and disposal and folpet degrades rapidly in air due to reaction with hydroxyl radicals with a half-life between 6.16 hours (QSAR estimation) and 1.02 days (EPA AOP v1.92 model based on 0.5×10^6 OH/cm^3 and a 24 hour day). In the absence of exposure to air-borne residues, non-target organisms are considered not to be at risk from folpet in the atmosphere and a detailed assessment of risk is therefore not presented for the atmospheric compartment.

Thiophosgene

One of the products formed in the breakdown of folpet is thiophosgene ($SCCl_3$), however its

tendency to hydrolyse rapidly and its high reactivity with other substances likely to be present in wash-waters, leachates, drains and sewers mean that it is unstable and that exposure of biota in aquatic and terrestrial compartments of the environment to thiophosgene will not occur. Thiophosgene is therefore not considered to be an environmentally relevant degradate of folpet. Carbon dioxide is ultimately formed from the thio(trichloromethyl) side chain and at higher pH values this tends to remain in solution as carbonate. The intermediate degradates from the thio(trichloromethyl) side chain have not been identified but it is postulated in the EFSA review report for folpet that these intermediates are the sodium salt of trichloromethylsulfenic acid and trichloromethylmercaptan.

2.2.2.2. Effects assessment

Aquatic organisms

Aquatic ecotoxicology studies performed with folpet have been conducted with exposure regimes that fall into two types.

The first type entails exposure under flow-through or semi-static conditions (in the latter case with a short interval between media renewals), with the aim of counteracting hydrolysis and maintaining consistent exposure to the active substance at concentrations at or near nominals and in accordance – in this respect – with conventional test guideline requirements. These tests provide endpoints that serve to establish the intrinsic toxicity of folpet to aquatic biota and they fulfil the requirements for the classification of the active substance.

The second type entails exposure under static or static renewal conditions (in the latter case with an extended interval between media renewals), whereby the concentration of folpet declined as a result of hydrolysis, either unavoidably because of the practical constraints of the test design (e.g. algal studies, where flow-through or semi-static exposure regimes cannot be implemented for technical reasons) or deliberately, as in the case of static acute fish tests, where the exposure pattern was intended to simulate intermittent episodes of unintended surface water contamination via direct spray drift inputs potentially arising from the use of folpet as a plant protection product. In these studies exposure would have been to the hydrolysis products of folpet for most of the test duration, following a brief initial phase of exposure to the active substance. Some chronic toxicity studies were performed similarly, with a regime of semi-static media renewal, but with the renewals performed at intervals of e.g. 7 days to represent worst-case agricultural practice (*i.e*. the regime with the shortest separation between treatments), so that the exposure was also to the hydrolysis products for most of the time, punctuated by short, transient spikes of exposure to folpet a.s. at test initiation and immediately following each renewal.

In the acute timescale, fish were marginally the most sensitive group of aquatic organisms to the parent active substance. *O. mykiss* was identified as the most sensitive species in the flow-through toxicity tests (96-hour LC_{50}: 15 µg a.s./L, mean measured), however 96-hour LC_{50} endpoints of 233 and 1260 µg folpet-equiv/L (nominal) were obtained for the same species under static conditions. The lowest fish 96-hour LC_{50} for fish under static conditions was 98 µg folpet-equiv/L (*S. trutta*). The similarity of the 24-hour and 96-hour LC_{50} values in the static acute toxicity study *O. mykiss* indicates an absence of latency; *i.e*. most of the mortality occurred during the initial phase of exposure to folpet. This effect is replicated in the other acute, static tests with other fish species, implying that the hydrolysis degradates of folpet are less acutely toxic to fish than the parent active substance. This is confirmed by acute toxicity studies performed with fish exposed to phthalimide, phthalic acid, phthalamic acid, benzamide and 2-cyanobenzoic acid that gave 96-hour LC_{50} endpoints in the range 38000 to > 100000 µg/L. All the relevant degradation products of folpet that may be formed by various processes – including hydrolysis – are therefore less acutely toxic to fish than the parent active substance, by several orders of magnitude.

Similar results have been obtained in studies with aquatic invertebrates. *D. magna* was the most sensitive invertebrate species in flow-through acute toxicity tests (48-hour EC_{50}: 20 µg

a.s./L, mean measured), whereas a 48-hour EC_{50} of > 1460 µg folpet-equiv/L (mean measured initial concentration) was provided by a study performed with *D. magna* under static conditions. By comparison, acute EC_{50} endpoints for *D. magna* exposed to phthalimide, phthalic acid, phthalamic acid, benzamide and 2-cyanobenzoic acid range from 39000 to > 100000 µg/L, demonstrating that the degradation products of folpet – including those that are formed by hydrolysis - are markedly less acutely toxic to aquatic invertebrates than the parent compound.

Comparable trends are evident in the outcomes of long-term aquatic toxicity studies. *D. magna* was the most sensitive sensitive species to folpet under flow-through conditions (21 day NOEC: 1.8 µg a.s./L, mean measured. In a semi-static 21-day study a NOEC of 55 µg/L was obtained for the same species with regime of a 7-day interval between media renewals. Fish exhibited similar responses. NOEC values of 11 and 8.1 µg folpet/L (mean measured) were obtained for *P. promelas* in two early life stage studies conducted under flow-through conditions, whereas a growth test with juvenile *O. mykiss* exposed to folpet under semi-static conditions (three media renewals/week) provided a 28-day LC_{50} of 110 µg a.s./L, nominal (a higher value than the flow-through acute endpoint for the same species) and a NOEC of 19 µg folpet/L. The difference in long-term NOECs for fish between the studies that employed flow-through and semi-static exposure appears relatively small compared to that indicated for invertebrates, however this is a reflection of the higher frequency of media renewal and hence longer exposure to intact folpet a.s. that occurred in the 28-day *O. mykiss* study, compared to the 21-day semi-static reproduction test with *D. magna*.

Algal growth inhibition studies are necessarily conducted under static conditions and the active substance rapidly dissipated in the study of the effects of folpet on *D. subspicatus*. The 72-hour E_rC_{50} and corresponding NOEC values were > 10000 and 700 µg a.s./L (nominal). Similar studies performed with *P. subcapitata* exposed to phthalic acid, phthalamic acid, benzamide and 2-cyanobenzoic acid gave 72-hour E_rC_{50} endpoints in the range > 10000 to > 100000 µg/L. The relevant products of folpet dissipation therefore exhibit low toxicity to algae.

No studies have been performed to determine the chronic aquatic toxicity of the individual metabolites of folpet in isolation, however it is likely that they are each much less toxic than the parent active substance, mirroring the differential evident between folpet and its degradates in terms of their acute aquatic toxicity endpoints. The reduction in toxicity of folpet observed in long-term studies that employed static-renewal exposure conditions (where the parent active substance would have undergone rapid hydrolysis), compared to that seen in studies where flow-through conditions were employed, is qualitatively similar to the differences seen in the acute toxicity endpoints. This supports the contention that the chronic aquatic toxicity of the hydrolysis degradates is also much lower than that of folpet a.s.

Intact folpet a.s. is not expected to enter the aquatic compartment of the environment following its proposed uses in PT7. The potential exposure of aquatic biota is expected to be limited to folpet degradates, which all have a low K_{OC} (modelled EPISUITE KOCWIN estimates for phthalimide, phthalic acid, phthalamic acid, benzamide and 2-cyanobenzoic acid range from 1.2 to 80.9 L/kg), which implies a low affinity for organic matter. The environmentally relevant residues of folpet are therefore unlikely to partition to sediment and tests to determine the toxicity of folpet and its metabolites to sediment-dwelling organisms are therefore considered unnecessary and have not been performed.

Biological sewage treatment plant (STP) processes

Two studies with inocula from domestic catchment STPs have tested the effects of folpet on microbial processes involved in aerobic biological waste-water treatment. The first investigated the effect of folpet on the rate of oxygen uptake (total respiration, *i.e.* carbonaceous oxidation and nitrification combined) by activated sludge and the second specifically addressed effects on nitrifying microorganisms, which are generally the most sensitive group. The test systems were dosed with direct additions of folpet a.s. and

although some hydrolysis will have occurred under the test conditions, the endpoints provided by these tests reflect an initial exposure to the parent active substance that represents the highly improbable worst-case compared to the likely exposure of STP microflora in the context of the proposed uses of folpet in PT7. The 3-hour EC_{50} and NOEC for inhibitory effects of folpet on activated sludge respiration (OECD 209) were > 320 and 10 mg folpet/L (nominal), respectively. The 4-hour EC_{50} and NOEC for inhibition of nitrification in activated sludge (ISO 9509) were > 1000 and 32 mg folpet (nominal), respectively. These outcomes indicate that nitrification is not more susceptible to inhibition by folpet than the carbonaceous respiration processes of heterotrophic microorganisms.

Terrestrial organisms

The 14-day LC_{50} of folpet to *E. foetida* was greater than 1000 mg/kg dry soil, equivalent to > 882 mg a.s./kg on a wet weight basis. The sublethal effects of folpet were assessed using two formulations of folpet (a suspension concentrate (SC) and a water dispersible granule (WDG)), both containing nominally 80% folpet. The lowest NOEC for sublethal effects was reported to be 5.18 mg folpet-equiv/kg dry soil, converted from the test treatments expressed in terms of application rates, incorporation to depth of 5 cm and a dry soil bulk density of 1500 kg/m^3. This corresponds to a value of 4.57 mg folpet-equiv/kg wet soil, assuming a moist soil density of 1700 kg/m^3 as prescribed by the EU TGD.

The inhibition of soil microbial function in the presence of a suspension concentrate (SC) plant protection product containing folpet was tested under laboratory conditions in two field soils over a period of 63 days, with intermediate measurements made after 3 hours and 14 and 28 days. Two treatments based on agricultural application rates were used, equating to concentrations of 1.062 and 10.62 mg folpet/dry soil, converted from the applied rates by assuming incorporation to depth of 10 cm and a dry soil bulk density of 1500 kg/m^3. These concentrations correspond to values of 0.937 and 16.54 mg folpet-equiv/kg wet soil, assuming a moist soil density of 1700 kg/m^3 as prescribed by the EU TGD. Nitrifying activity indicated by the formation of oxidised inorganic nitrogen (nitrite and nitrate combined) diverged from the untreated control by less than ±10% at both folpet concentrations in both soils and at all timepoints. There was no consistent dose-response in the magnitude of the effect. Dehydrogenase activity was suppressed to similar extents throughout the incubation in both soils and the effect was consistently greater at the higher folpet concentration. After 28 days, dehydrogenase activity was reduced by 1.6% and 2.9% relative to the untreated controls at the lower folpet concentration and by 14.6% and 17.5% at the higher. The overall NOEC for effects on the activity of soil microflora is therefore set at 0.937 mg folpet-equiv/kg wet soil, where suppression of nitrification and dehydrogenase activity after 28 days remained below 10%.

It is expected that the relevant metalites of folpet were formed in moist soil under the conditions of the laboratory tests performed with the active substance, and that their influence is therefore accommodated in the endpoints reported for folpet a.s. Based on the evidence provided by the aquatic toxicity studies, the relevant metabolites of folpet are expected to be less toxic than the parent active substance.

Further studies have been performed to address the long-term toxicity of the hydrolysis metabolites phthalimide and phthalic acid to representatives of three groups of terrestrial organisms: earthworms, soil microflora and terrestrial plants. The soil microflora studies investigated the effect of each metabolite on carbon transformation, based on the findings of the OECD 209 and ISO 9509 studies performed with activated sludge which showed that nitrogen transformation was less susceptible to inhibition by folpet than combined respiratory processes. The terrestrial plant studies addressed the effects of soil-mediated exposure on seed germination and seedling development of two monocot and four dicot species.

The lowest long-term endpoint for phthalimide is the 28-day earthworm NOEC of 56.7 mg/kg dry artificial soil. The soil used in the study contained the standard 10% organic matter (peat), however the adsorption/desorption coefficient of phthalimide has been estimated in five soils of European origin using the batch equilibrium method, with Koc

values determined for phthalimide in the range 55.7 to 293.1 mL/g. Phthalimide therefore has a low tendency to bind to organic matter and the test conditions employed in this study are unlikely to have resulted in under-estimation of the long-term toxicity of phthalimide to earthworms. Adjustment of the endpoint to compensate for the unusually high organic matter content of the test soil is considered to be unnecessary.

Assuming a dry soil bulk density of 1500 kg/m^3, the earthworm long-term NOEC of 56.7 mg/kg dry soil corresponds to 50.03 mg phthalimide/kg wet soil with a bulk density of 1700 kg/m^3 as prescribed by the EU TGD.

The lowest long-term endpoint for phthalic acid is the calculated EC_{10} of 44.3 mg/kg based on a reduction in the fresh weight of cropped biomass of *D. carota* seedlings in an emergence and seedling development study. (The calculated EC_{10} undercuts the corresponding NOEC of 64 mg/kg dry soil for the same species). The soil used was LUFA 2.2, classified (DIN) as a loamy sand soil with a carbon content of 1.77%. The adsorption/desorption coefficient of phthalic acid estimated by the KOCWIN model in EPISUITE is 80.85 L/kg and the model database contains an experimentally determined log K_{OC} value of 1.07. Phthalic acid therefore has a low tendency to bind to organic carbon. The test conditions employed in this study are consequently unlikely to have resulted in under-estimation of the potential effects of phthalic acid on soil-mediated exposure of terrestrial plants at the sensitive germination and root/shoot development stages. Adjustment of the endpoint to compensate for the organic matter content of the test soil is unnecessary.

Assuming a dry soil bulk density of 1500 kg/m^3, the EC_{10} of 44.3 mg/kg dry soil corresponds to 39.09 mg phthalic acid/kg wet soil with a bulk density of 1700 kg/m^3 as prescribed by the EU TGD.

Effects of folpet on other terrestrial organisms

Toxicity endpoints are also available from studies performed with other groups of terrestrial organisms although their exposure is not foreseen following the use of folpet in PT7. These are outlined below.

No mortalities or treatment-related abnormalities were observed in an acute toxicity test with honey bees (*A. mellifera*). The acute LD_{50} endpoints for contact and oral exposure were > 200 and > 236 µg folpet/bee, respectively.

Folpet was applied post-emergence (direct foliar exposure) as a water-dispersible plant protection product formulation to a range of crops (monocots and dicots) in a field study, with single applications at rates of up to 8.0 kg a.s./ha. There were no observations of phytotoxicity or effects on plant vigour.

Folpet exhibited low acute oral and short-term dietary toxicity to birds. The acute oral LD_{50} of folpet to bobwhite quail was greater than 2510 mg/kg bw (males and females). The no-effect level (NOEL) was 631 mg/kg bw, based on a slight, initial decrease in body weight at 1000 mg./kg bw and above, followed by a compensatory increase in body weight by the end of the test. The short-term dietary LC_{50} of folpet to bobwhite quail was greater than 5000 mg/kg diet. The NOEC was also 5000 mg/kg diet, based on an absence of effect at the single concentration tested. The short-term dietary LC_{50} of folpet to mallard duck was greater than 5000 mg/kg diet. The NOEC was also 5000 mg/kg diet, based on an absence of effect at the single concentration tested.

An eight week screening study with bobwhite quail indicated that there were no significant effects on adult birds or on reproductive performance up to a concentration of 4640 mg folpet/kg diet. In one-generation reproduction studies with bobwhite quail and mallard duck there were no significant effects on reproductive parameters at 1000 mg a.s./kg diet, the highest concentration tested. In both studies there were slight, significant effects on hatchling body weight at 100 mg a.s./kg diet and above, however these were slight and inconsistent and unrelated to dose. In the mallard duck study there were slight significant

reductions in adult food consumption at 100 to 1000 mg a.s./kg diet. These were considered to be unrelated to treatment as there were no permanent treatment-related effects on adult body weight and food consumption reductions occurred inconsistently. The long-term NOEC for folpet is 1000 mg a.s./kg diet.

2.2.2.3. PBT and POP assessment

Persistence

Since folpet can be classified as readily biodegradable, is degraded in aquatic systems with a DT_{50} value of ca 0.4 hours and is also degraded in soil with a DT_{50} value of less than 4.3 days, it cannot be considered to fulfil the P criterion.

Bioaccumulation

The B criterion in the TGD is fulfilled when a substance has a bioconcentration factor (BCF) of > 2000 or, if BCF data is not available, when the log Kow > 4.5. The highest recorded BCF value for folpet is 56, measured in whole fish, which is lower than the limit value of 2000. Since a BCF value is available and below the limit value, folpet cannot be considered to fulfil the B criterion.

Toxicity

The T criterion used in the TGD is a chronic NOEC for aquatic organisms of < 0.01 mg/L or, if no long-term data is available, the criterion is $L(E)C_{50}$ to aquatic organisms < 0.1 mg/L. For mammals, the T criterion is fulfilled when the substance is classified as carcinogenic (Cat 1 or 2), mutagenic (Cat 1 or 2) or toxic for reproduction (Cat 1, 2 or 3) or when there is evidence of chronic toxicity.

The long-term effects of folpet have been determined for fish (two early life-stage studies) and for *D. magna* with NOEC values of 8.1 to 11 µg/L and 2.1 µg/L, respectively. However, these studies were conducted under flow through conditions. Due to the rapid hydrolysis of folpet there is no potential for prolonged exposure of aquatic organisms and therefore studies conducted under flow through conditions are not considered to represent realistic exposure in the environment and therefore the end points should not set these studies. From static tests the lowest fish (*S. trutta*) 96-hour LC_{50} was 98 µg folpet/L.

Based on consideration of intrinsic toxicity, without taking account of realistic exposure, the worst case NOEC value is < 0.01 mg/L and the worst-case LC_{50} is < 0.1 mg/L. Folpet is therefore considered to fulfil the T criteria for aquatic organisms.

It should be noted that folpet is rapidly hydrolysed under environmental conditions and that its metabolites are relatively non-toxic compared to the parent active substance. Short term L/EC_{50} endpoints for fish, invertebrates and algae for phthalimide, phthalic acid, phthalamic acid, benzamide and 2-cyanobenzoic acid all range from > 10 mg/L to > 100 mg/L. The hydrolysis products of folpet do not fulfil the criteria for classification in the aquatic environment.

Folpet is not classified as carcinogenic (Cat 1 or 2), mutagenic (Cat 1 or 2) or toxic for reproduction (Cat 1, 2 or 3). However, results from a chronic exposure to mice indicated potential for inducing gastric carcinomas although this effect was not replicated in rats and there is no evidence for folpet induced human carcinogenicity. Folpet does not show evidence of chronic toxicity, as identified by the classifications T, R45, R48, R60 and R61 or Xn, R48, R62, R63 and R64. The toxicity of folpet to mammals is low, with an LD50 for rat of >2,000 mg/kg bw.

Since none of the above toxicological thresholds are met, folpet is not considered to fulfil the T criterion for mammals.

POP
Folpet is a solid with a relatively high melting point and low vapour pressure and can therefore be considered as non-volatile. Concentrations in air are expected to be negligible during use and disposal and folpet degrades rapidly in air due to reaction with hydroxyl radicals with a half-life between 6.16 hours (QSAR estimation) and 1.02 days (EPA AOP v1.92 model based on 0.5×10^6 OH/cm^3 and a 24 hour day). Based on this information folpet is not considered to be a persistent organic pollutant.

2.2.2.4. Exposure assessment

Aquatic
The uses considered for folpet in PT7 applications provide no potential for direct entry of the active substance into the aquatic compartment.

The biocidal uses of folpet are expected to result in the discharge of folpet residues into drains and sewers and subsequent transport to sewage treatment plants (STPs). In reality, the biocidal uses of folpet will generate effluents in which the parent active substance is completely hydrolysed before and/or during biological treatment: either in-use, during transport in the drain/sewer system or during primary settlement of the STP influent before entering the secondary (biological) treatment phase. The hydraulic retention time of influents through secondary treatment at STPs, followed by settlement prior to discharge of the final, treated effluent to the receiving water course is in the order of several hours. Given that the hydrolysis DT_{50} of folpet is measured in minutes and that folpet is expected already to be hydrolysed before it reaches secondary treatment processes, it may be assumed (regardless of the degree to which folpet and its hydrolysis products may be biodegraded during biological treatment) that no parent active substance will be present in final STP effluents at the point at which they are discharged into receiving waters. Consequently, exposure of aquatic biota to the intact parent active substance is not expected to occur following the proposed uses in PT7 that entail drain disposal followed by STP. Exposure will instead be to the principal hydrolysis degradates rather than folpet itself.

Alternatively, releases may occur by weathering and leaching processes from – for example – surfaces painted with coatings containing folpet, or from films, sealants or plastic items containing folpet. In these situations, however, the processes are expected to be gradual and to occur only when the relevant surfaces are wetted. Rapid hydrolysis will occur in tandem with the leaching process. Exposure of biota in surface waters receiving such leachates will therefore be to the principal hydrolysis degradates of folpet rather than to the active substance itself.

Terrestrial
Folpet residues that become bound to sludge solids during waste-water treatment may enter the soil compartment if STP sludge is applied to land. However, bearing in mind the rationale provided above, the residues in STPs will be folpet degradates rather than the parent active substance. Moreover, modelled K_{OC} values for the breakdown intermediates of folpet are all relatively low and also lower than that of folpet a.s., suggesting that the degradates have only a weak affinity for organic matter and STP sludge, and that this indirect route is therefore unlikely to result in significant contamination of soil with folpet residues.

Alternatively, releases may occur by weathering and leaching processes from – for example – surfaces coated with paint treated with folpet, or from films, sealants or plastic items containing folpet. In these situations, however, the processes are expected to be gradual and to occur only when the relevant surfaces are wetted. Rapid hydrolysis of folpet will occur in tandem with the leaching process. Exposure of biota in surface run-off soak-away systems and soils receiving such leachates will therefore be to the principal hydrolysis degradates of folpet rather than to the active substance itself.

Releases of folpet may occur also during the application of the formulated product.

Environmental risk in the aquatic compartment (incl. sediment)

Given the exposure considerations that are outlined above, the environmental risk assessment for the aquatic compartment needs to take account of the facts that:

a) the exposure arising from the various PT7 biocidal uses of folpet is continuous and therefore chronic in character, and;

b) since none of the biocidal uses of folpet facilitates direct entry of the active substance into surface waters, exposure will be to foplet's hydrolysis metabolites rather than the intact parent active substance.

Consequently the PNEC for the aquatic compartment must be derived from chronic aquatic toxicity endpoints to correspond to the relevant environmental exposure. These entities have not been tested individually and chronic toxicity endpoints are therefore unavailable for each of the relevant metabolites. Toxicity data are available that show that the metabolites of folpet are several orders of magnitude less acutely toxic to fish and invertebrates (which are both much more sensitive than algae) than the parent compound and it would be reasonable to expect that the metabolites are also substantially less toxic to aquatic biota than folpet a.s. following long-term exposure.

Of the available data, the most appropriate basis for the PNEC derivation are therefore the endpoints provided by long-term studies conducted with folpet, but under static-renewal conditions where the renewal interval was long enough to permit complete hydrolysis of the active substance. The pattern of exposure achieved under these conditions would therefore have been to the hydrolysis products of folpet for most of the test duration, punctuated by brief, transient phases of exposure to folpet immediately after test initiation and each media renewal. Since folpet was intermittently present in these test regimes, the observed toxicity is considered to have been greater than it would have been had the exposure been to the hydrolysis products alone, and from the point of view of representing long-term metabolite toxicity these endpoints are therefore worst-case. The conservatism of this approach is indicated by the acute toxicity data set, where endpoints obtained for folpet under static conditions that permitted hydrolysis were (albeit higher than) still closer to those of folpet when tested under flow-through conditions, than to the very much higher endpoints for each of the metabolites tested individually.

Consequently the PNEC derived from end points provided by the static-renewal studies dosed with folpet is considered to be highly protective with respect to the exposure that is expected to occur in the aquatic compartment following the biocidal uses of folpet in PT7.

Surface water ($PNEC_{water}$)

As noted above, since no long-term endpoints are available for the relevant metabolites of folpet, the data that serve as the most appropriate basis for the PNECwater derivation are NOECs provided by long-term studies conducted with folpet, but under static-renewal conditions where the renewal interval was long enough to permit complete hydrolysis of the active substance. The relevant values are presented in the table below.

Key long-term aquatic toxicity endpoints for folpet used to derive $PNEC_{water}$

Test organism	Time-scale, exposure regime	Endpoint	Toxicity (µg/L)
Fish			
Oncorhynchus mykiss	28 days (s-s)[a], 3 renewals/week	NOEC	19 (nom)
Invertebrates			
Daphnia magna	21 days (s-s)[a], 7 d renewal	NOEC	55 (m.m.i.)

Test organism	Time-scale, exposure regime	Endpoint	Toxicity (µg/L)
Algae			
Desmodesmus subspicatus	72 hours (s)[b]	NOEC	700 (nom.)

s: static exposure;
s-s: semi-static exposure;
m.m.i. based on mean measured initial concentration(s);
nom. based on nominal concentrations;
[a] folpet allowed to hydrolyse, exposure mainly to hydrolysis degradates, with brief exposure to a.s. at test initiation and following each media renewal.
[b] folpet allowed to hydrolyse, exposure mainly to hydrolysis degradates following brief initial exposure to a.s.

Since long-term NOECs are available for different species representing three different trophic levels, the $PNEC_{water}$ is derived by applying an assessment factor of 10 to the lowest endpoint value, in accordance with the EU TGD on environmental risk assessment. Hence:

$PNEC_{water}$: 19/10 = **1.9 µg folpet/L**

The exposure achieved under the conditions of the test that provides the key endpoint used to calculate $PNEC_{water}$ will have been to the hydrolysis products of folpet for most of the test duration, punctuated by brief, transient phases of exposure to folpet immediately after test initiation and each media renewal. Since folpet was intermittently present in this test regime, the observed toxicity is considered to be greater than it would have been had the exposure been to the hydrolysis products alone, and from the point of view of representing long-term metabolite toxicity this endpoint is therefore worst-case.

Consequently the $PNEC_{water}$ of 1.9 µg folpet/L derived above - particularly as it stems from a study re-dosed with folpet on three occasions per week - is considered to be highly protective with respect to the exposure that is expected to occur in the aquatic compartment following the biocidal uses of folpet in PT7.

Sediment compartment ($PNEC_{sediment}$)

Intact parent folpet a.s. is not expected to reach the aquatic environment for the reasons given above. Moreover, given the very short residence of folpet in water/sediment systems, that the water and sediment metabolites have been shown to be significantly less toxic than the parent folpet and that any sediment partitioned residues are principally bound and are unlikely to be folpet, a toxicity study with a sediment dwelling insect is not considered relevant to the risk assessment for products with folpet as the sole active substance. Therefore, the risks to sediment-dwelling organisms are considered to be adequately covered by the assessment for the aquatic compartment based on PNECwater.

However a $PNEC_{sediment}$ estimate can be derived using equation (70) provided in the EU TGD for environmental risk assessment, with input parameters of 0.0019 mg/L for PNECwater and 304 L/kg for the adsorption coefficient of folpet. Hence:

$PNEC_{sediment}$ = 2900 µg folpet/kg wet weight

Sewage treatment plant ($PNEC_{STP}$)

According to the EU TGD on environmental risk assessment, the $PNEC_{STP}$ may be derived by applying an assessment factor to the NOEC values from relevant tests. An AF of 10 is used in conjunction with the NOEC from tests of inhibition of respiration of activated sludge (representing combined carbonaceous and nitrogenous oxidation processes), whereas a lower AF of 1.0 is applied to the NOEC of specific tests of nitrification inhibition in activated

sludge, since nitrifying microorganisms are generally the most sensitive. In the case of folpet, however, the activated sludge respiration test provides the lowest NOEC. Nevertheless, in accordance with the TGD the PNEC was derived as follows:

$PNEC_{STP}$: 10000/10 = **1000 µg folpet/L**

Environmental risk in the terrestrial compartment

Given the exposure considerations that are outlined above, the environmental risk assessment for the terrestrial compartment needs to take account of the facts that any exposure arising from the various PT7 biocidal uses of folpet will be continuous and therefore chronic in character

Consequently the PNEC for the terrestrial compartment must be derived from chronic terrestrial toxicity endpoints to correspond to the relevant environmental exposure. It is expected that the relevant metabolites of folpet were formed in moist soil under the conditions of the laboratory tests performed with the active substance and that their influence is therefore accommodated in the endpoints reported for folpet a.s. Aquatic toxicity data are available that show that the metabolites of folpet are several orders of magnitude less acutely toxic to fish and invertebrates (which are both much more sensitive than algae) than the parent compound and it would be reasonable to expect similar trends for terrestrial organisms whereby the metabolites are also substantially less toxic to terrestrial biota than folpet a.s. and that a similar trend also holds for long-term exposures.

Consequently the PNECsoil derived from end points provided by the studies dosed with folpet is considered to be highly protective with respect to the exposure that is expected to occur in the terrestrial compartment following the biocidal uses of folpet in PT7.

Further studies have been performed to address the long-term toxicity of the hydrolysis metabolites phthalimide and phthalic acid to representatives of three groups of terrestrial organisms: earthworms, soil microflora and terrestrial plants. The soil microflora studies investigated the effect of each metabolite on carbon transformation, selected on the basis on the findings of the OECD 209 and ISO 9509 studies performed with activated sludge which showed that nitrogen transformation was less susceptible to inhibition by folpet than combined respiratory processes. The terrestrial plant studies examined the effects of soil-mediated exposure on seed germination and seedling development of two monocot and four dicot species.

Effects of phthalimide on soil organisms

Organism/ activity	Endpoint	Result
Effects on earthworm reproduction (OECD 222, DIN ISO 11268-2).	28-day NOEC	56.7 mg/kg dry artificial soil (nom.)
Inhibition of glucose –induced respiration (C-transformation) (OECD 217).	28-day NOEC	1000 mg/kg dry LUFA 2.3 soil (nom.)
Seedling emergence and seedling development of six terrestrial plant species (OECD 208). Most sensitive endpoint: shoot biomass; most sensitive species: *B. vulgaris*).	Lowest EC_{10}	58.5 mg/kg dry LUFA 2.2 soil (nom.)

The lowest long-term endpoint for phthalimide is the 28-day NOEC of 56.7 mg/kg dry artificial soil. The soil used in the study contained the standard 10% organic matter (peat), however the adsorption/desorption coefficient of phthalimide has been estimated in five soils of European origin using the batch equilibrium method, with Koc values in the range 55.7 to 293.1 mL/g. Phthalimide therefore has a low tendency to bind to organic matter and the test conditions employed in this study are unlikely to have resulted in under-

estimation of the long-term toxicity of phthalimide to earthworms. Adjustment of the endpoint to compensate for the unusually high organic matter content of the test soil is considered to be unnecessary.

Assuming a dry soil bulk density of 1500 kg/m^3, the earthworm long-term NOEC 56.7 mg/kg dry soil corresponds to 50.03 mg/kg wet soil with a bulk density of 1700 kg/m^3 as prescribed by the EU TGD.

Based on the availability of long term endpoints for three species or groups of organisms representing three different trophic levels, a PNEC may be calculated for phthalimide by applying an assessment factor of 10 to the lowest NOEC:

$PNEC_{soil}$: 50.03/10 = **5.003 mg phthalimide/kg wet soil**

Effects of phthalic acid on soil organisms

Organism/ activity	**Endpoint**	**Result**
Effects on earthworm reproduction (OECD 222, DIN ISO 11268-2).	28-day NOEC	56.7 mg/kg dry artificial soil (nom.)
Inhibition of glucose –induced respiration (C-transformation) (OECD 217).	28-day NOEC	400 mg/kg dry LUFA 2.3 soil (nom.)
Seedling emergence and seedling development of six terrestrial plant species (OECD 208). Most sensitive endpoint: shoot biomass; most sensitive species: *D. carota*).	Lowest EC_{10}	44.3 mg/kg dry LUFA 2.2 soil (nom.)

The lowest long-term endpoint for phthalic acid is the calculated EC_{10} of 44.3 mg/kg based on a reduction in the fresh weight of cropped biomass of *D. carota* seedlings in an emergence and seedling development study. (The calculated EC_{10} undercuts the corresponding NOEC of 64 mg/kg dry soil for the same species). The soil used was LUFA 2.2, classified (DIN) as a loamy sand soil with a carbon content of 1.77%. The adsorption/desorption coefficient of phthalic acid estimated by the KOCWIN model in EPISUITE is 80.85 L/kg and the model database contains an experimentally determined log K_{OC} value of 1.07. Phthalic acid therefore has a low tendency to bind to organic carbon. The test conditions employed in this study are consequently unlikely to have resulted in under-estimation of the potential effects of phthalic acid on soil-mediated exposure of terrestrial plants at the sensitive germination and root/shoot development stages. Adjustment of the endpoint to compensate for the organic matter content of the test soil is unnecessary.

Assuming a dry soil bulk density of 1500 kg/m^3, the EC_{10} of 44.3 mg/kg dry soil corresponds to 39.09 mg/kg wet soil with a bulk density of 1700 kg/m^3 as prescribed by the EU TGD.

Based on the availability of long term endpoints for three species or groups of organisms representing three different trophic levels, a PNEC may be calculated for phthalic acid by applying an assessment factor of 10 to the lowest NOEC:

$PNEC_{soil}$: 39.09/10 = **3.909 mg phthalic acid/kg wet soil**.

Endpoints are also available from other tests performed with insects (bees), plants and vertebrates (birds) to address the requirements of the uses of folpet in the plant protection sector and indicate that folpet has low intrinsic toxicity to these groups of organisms. However these involve exposure routes other than via soil and are therefore not relevant to the PT7 biocidal uses of folpet, or are expressed in terms that cannot be related to concentrations in soil. These endpoints have therefore not been taken into account in the derivation of $PNEC_{soil}$.

The terrestrial exposure assessment for folpet as a PT7 biocidal active substance was performed using the PT8 and PT10 release scenarios as discussed above for the aquatic environment. A range of values were obtained for folpet, depending on the model selected and either resulted from leaching, run-off and down the drain processed (with release to soil via STP), or direct exposure of soil close to the treatment site (surrogate scenarios include e.g house façade, fence post). The tonnage distribution model was also used as a comparative method of PEC calculation.

For the STP route, using the maximum possible exposure values (and therefore a worst-case risk assessment) the soil PEC:PNEC ratios were less than one. The risk assessment according to this scenario therefore demonstrates that the risk to terrestrial organisms from folpet is acceptable.

For the direct exposure route, the inital soil PEC:PNEC ratios in the soil environment immediately adjacent to treated surfaces were greater than one. With increased distance and accounting for degradation in the soil the apparent risk to soil organisms is considerably reduced. Although a potential risk to terrestrial organisms is indicated the risk is considered acceptable due the highly conservative and localised nature of the PEC calculation and the very low persistence of the active substance.

Environmental risk in the atmospheric compartment

The vapour pressure of folpet at a temperature of 25°C (as determined by USEPA 63-9 guideline) is 2.1×10^{-5} Pa and Henry's law constant is 8×10^{-3} $Pa.m^3.mol^{-1}$ (based on a water solubility of 0.8 mg/L). Therefore folpet is not considered volatile and is not expected to volatilise to air in significant quantities. Furthermore, the photochemical oxidative degradation half-life of folpet in air was estimated using the Atmospheric Oxidation Program v1.90 (AOPWIN), which is based on the structural activity relationship (QSAR) methods developed by Atkinson, R (1985 to 1996). The estimated half-life of folpet in air via hydroxyl reactions is not expected to exceed 6.16 hours. Therefore, even if present, folpet is not expected to persist in air. In the absence of exposure to air-borne residues, non-target organisms are considered not to be at risk from folpet in the atmosphere and a detailed assessment of risk is therefore not presented for the atmospheric compartment.

Secondary poisoning

The log K_{OW} of folpet is 3.017. Based on a laboratory study, in which bluegill sunfish were exposed to folpet, the whole fish BCF was 56 with a DT_{50} for depuration of 0.63 days (indicating rapid depuration). The low BCF value of folpet indicates that the risks of secondary poisoning are expected to be very low.

Summary of PNECs

Compartment	PNEC
Surface water	1.9 µg folpet/L
Sediment	2900 µg folpet/kg wet weight
STP	10000 µg folpet/L
Atmosphere	Not relevant
Soil	37.5 µg folpet/kg wet soil
	5003 µg phthalimide/kg wet weight
	3909 µg phthalic acid/kg wet weight

2.2.2.5. Risk characterisation

The exposure assessment for folpet as a PT7 biocidal active substance was performed using the PT8 and PT10 release scenarios as surrogate exposure models. These models considered exposure of the environment via application of the formulated product, or leaching from treated surfaces during service life, including run-off to drain and STP. The use of PT8 and PT10 scenarios was required in response to Member State comments on the draft CAR. The PEC values in surface water, sediment, STP and soil were calculated using these scenarios and the standardised procedures incorporated within the EUSES 2.1 model. The tonnage distribution model was also used as a comparative method of PEC calculation. The emission scenarios for outdoor spray application of wood preservatives (PT8) presented in the OECD Revised Emission Scenario Document for Wood Preservatives (September 2013) was used as surrogate exposure scenarios for outdoor application of paint. The considered service life (time 2) was 5 years.

A range of values was obtained for folpet and the major metabolites phthalimide and phthalic acid in soil, depending on the model selected. The maximum exposure values obtained were used in order to present a worst-case risk assessment.

PEC/PNEC ratios for freshwater (via the STP) exposed to folpet following PT7 uses

Scenario	PECs (mg/L)	PNEC (mg/L)	PEC/PNEC
Folpet			
Maximum exposure based on **PT8** exposure scenarios (Noise barrier)	2.14×10^{-4}	1.90×10^{-3}	0.11
Maximum exposure based on **tonnage** distribution	4.30×10^{-5}	1.90×10^{-3}	0.02
PT10 Brushing scenario during application	2.698×10^{-5}	1.90×10^{-3}	0.0142
PT10 Brushing scenario service life time 1	0.0553	1.90×10^{-3}	29.1
PT10 Brushing scenario service life time 2	9.101×10^{-4}	1.90×10^{-3}	0.479
PT10 Spraying scenario during application	3.477×10^{-4}	1.90×10^{-3}	0.183
PT10 Spraying scenario service life time 1	0.0553	1.90×10^{-3}	29.1
PT10 Spraying scenario service life time 2	9.101×10^{-4}	1.90×10^{-3}	0.479
Phthalimide			
Maximum exposure based on PT8 exposure scenarios (Noise barrier)	4.63×10^{-4}	1.90×10^{-3}	0.24
Maximum exposure based on tonnage distribution	9.42×10^{-5}	1.90×10^{-3}	0.05
PT10 Brushing scenario during application	5.795×10^{-5}	1.90×10^{-3}	0.0305
PT10 Brushing scenario service life time 1	0.122	1.90×10^{-3}	**64.1**
PT10 Brushing scenario service life time 2	1.995×10^{-3}	1.90×10^{-3}	**1.05**
PT10 Spraying scenario during application	7.505×10^{-4}	1.90×10^{-3}	0.395
PT10 Spraying scenario service life time 1	0.122	1.90×10^{-3}	**64.1**
PT10 Spraying scenario service life time 2	1.995×10^{-3}	1.90×10^{-3}	**1.05**
Phthalic acid			
Maximum exposure based on PT8 exposure scenarios (Noise barrier)	7.29×10^{-4}	1.90×10^{-3}	0.38
Maximum exposure based on tonnage distribution	9.16×10^{-5}	1.90×10^{-3}	0.05
PT10 Brushing scenario during application	5.624×10^{-5}	1.90×10^{-3}	0.0296
PT10 Brushing scenario service life time 1	0.117	1.90×10^{-3}	**61.6**
PT10 Brushing scenario service life time 2	1.919×10^{-3}	1.90×10^{-3}	**1.01**

Scenario	PECs (mg/L)	PNEC (mg/L)	PEC/PNEC
PT10 Spraying scenario during application	7.296×10^{-4}	1.90×10^{-3}	0.384
PT10 Spraying scenario service life time 1	0.117	1.90×10^{-3}	**61.6**
PT10 Spraying scenario service life time 2	1.919×10^{-3}	1.90×10^{-3}	**1.01**

PEC/PNEC rations for sediment (via STP) exposed to folpet following PT7 uses

Scenario	PECs (mg/kg)	PNEC (mg/kg)	PEC/PNEC
Folpet			
Maximum exposure based on **PT8** exposure scenarios (Noise barrier)	1.80×10^{-3}	2.9	<0.01
Maximum exposure based on **tonnage** distribution	3.61×10^{-4}	2.9	<0.01
PT10 Brushing scenario during application	2.259×10^{-4}	2.9	<0.01
PT10 Brushing scenario service life time 1	0.464	2.9	0.16
PT10 Brushing scenario service life time 2	7.627×10^{-3}	2.9	<0.01
PT10 Spraying scenario during application	2.929×10^{-3}	2.9	<0.01
PT10 Spraying scenario service life time 1	0.464	2.9	0.16
PT10 Spraying scenario service life time 2	7.627×10^{-3}	2.9	<0.01
Phthalimide			
Maximum exposure based on **PT8** exposure scenarios (Noise barrier)	8.63×10^{-4}	2.9	<0.01
Maximum exposure based on **tonnage** distribution	1.75×10^{-4}	2.9	<0.01
PT10 Brushing scenario during application	1.079×10^{-4}	2.9	<0.01
PT10 Brushing scenario service life time 1	0.227	2.9	0.0782
PT10 Brushing scenario service life time 2	3.741×10^{-3}	2.9	<0.01
PT10 Spraying scenario during application	1.398×10^{-3}	2.9	<0.01
PT10 Spraying scenario service life time 1	0.227	2.9	0.0782
PT10 Spraying scenario service life time 2	3.741×10^{-3}	2.9	<0.01
Phthalic acid			
Maximum exposure based on **PT8** exposure scenarios (Noise barrier)	4.45×10^{-4}	2.9	<0.01
Maximum exposure based on **tonnage** distribution	9.00×10^{-5}	2.9	<0.01
PT10 Brushing scenario during application	5.510×10^{-5}	2.9	<0.01
PT10 Brushing scenario service life time 1	0.115	2.9	0.396
PT10 Brushing scenario service life time 2	1.885×10^{-3}	2.9	<0.01
PT10 Spraying scenario during application	7.163×10^{-4}	2.9	<0.01
PT10 Spraying scenario service life time 1	0.115	2.9	0.396
PT10 Spraying scenario service life time 2	1.885×10^{-3}	2.9	<0.01
Scenario	**PECs (mg/L)**	**PNEC (mg/L)**	**PEC/PNEC**
Folpet surface water exposure			
Maximum exposure based on PT8 exposure scenarios	2.14×10^{-4}	1.90×10^{-3}	0.11
Maximum exposure based on tonnage distribution	4.30×10^{-5}	1.90×10^{-3}	0.02

Scenario	PECs (mg/kg)	PNEC (mg/kg)	PEC/PNEC
PT10 Brushing scenario during application	2.698×10^{-5}	1.90×10^{-3}	0.0142
PT10 Brushing scenario service life time 1	0.0553	1.90×10^{-3}	29.1
PT10 Brushing scenario service life time 2	9.101×10^{-4}	1.90×10^{-3}	0.479
PT10 Spraying scenario during application	3.477×10^{-4}	1.90×10^{-3}	0.183
PT10 Spraying scenario service life time 1	0.0553	1.90×10^{-3}	29.1
PT10 Spraying scenario service life time 2	9.101×10^{-4}	1.90×10^{-3}	0.479
Phthalimide surface water exposure			
Maximum exposure based on PT8 exposure scenarios	4.63×10^{-4}	1.90×10^{-3}	0.24
Maximum exposure based on tonnage distribution	9.42×10^{-5}	1.90×10^{-3}	0.05
PT10 Brushing scenario during application	5.624×10^{-5}	1.90×10^{-3}	0.0296
PT10 Brushing scenario service life time 1	0.117	1.90×10^{-3}	61.6
PT10 Brushing scenario service life time 2	1.919×10^{-3}	1.90×10^{-3}	1.01
PT10 Spraying scenario during application	7.296×10^{-4}	1.90×10^{-3}	0.384
PT10 Spraying scenario service life time 1	0.117	1.90×10^{-3}	61.6
PT10 Spraying scenario service life time 2	1.919×10^{-3}	1.90×10^{-3}	1.01
Phthalic acid surface water exposure			
Maximum exposure based on PT8 exposure scenarios	7.29×10^{-4}	1.90×10^{-3}	0.38
Maximum exposure based on tonnage distribution	9.16×10^{-5}	1.90×10^{-3}	0.05
PT10 Brushing scenario during application	5.795×10^{-5}	1.90×10^{-3}	0.0305
PT10 Brushing scenario service life time 1	0.122	1.90×10^{-3}	64.1
PT10 Brushing scenario service life time 2	1.995×10^{-3}	1.90×10^{-3}	1.05
PT10 Spraying scenario during application	7.505×10^{-4}	1.90×10^{-3}	0.395
PT10 Spraying scenario service life time 1	0.122	1.90×10^{-3}	64.1
PT10 Spraying scenario service life time 2	1.995×10^{-3}	1.90×10^{-3}	1.05

PEC/PNEC rations for STP exposed to folpet following PT7 uses

Scenario	PECs (mg/L)	PNEC (mg/L)	PEC/PNEC
Folpet			
Maximum exposure based on **PT8** exposure scenarios (Noise barrier)	2.14×10^{-3}	1	<0.01
Maximum exposure based on **tonnage** distribution	4.31×10^{-4}	1	<0.01
PT10 Brushing scenario during application	0.027	1	0.0269
PT10 Brushing scenario service life time 1	55.4	1	**55.4**
PT10 Brushing scenario service life time 2	0.91	1	0.91
PT10 Spraying scenario during application	0.349	1	0.349
PT10 Spraying scenario service life time 1	55.4	1	**55.4**
PT10 Spraying scenario service life time 2	0.91	1	0.91
Phthalimide			

Scenario	PECs (mg/L)	PNEC (mg/L)	PEC/PNEC
Maximum exposure based on **PT8** exposure scenarios (Noise barrier)	4.64×10^{-3}	1	<0.01
Maximum exposure based on **tonnage** distribution	9.42×10^{-4}	1	<0.01
PT10 Brushing scenario during application	0.001	1	<0.01
PT10 Brushing scenario service life time 1	1.220	1	**1.22**
PT10 Brushing scenario service life time 2	0.020	1	0.02
PT10 Spraying scenario during application	0.008	1	<0.01
PT10 Spraying scenario service life time 1	1.220	1	**1.22**
PT10 Spraying scenario service life time 2	0.020	1	0.02
Phthalic acid			
Maximum exposure based on **PT8** exposure scenarios (Noise barrier)	4.53×10^{-3}	1	<0.01
Maximum exposure based on **tonnage** distribution	9.16×10^{-4}	1	<0.01
PT10 Brushing scenario during application	0.001	1	<0.01
PT10 Brushing scenario service life time 1	1.170	1	**1.17**
PT10 Brushing scenario service life time 2	0.019	1	0.0192
PT10 Spraying scenario during application	0.007	1	<0.01
PT10 Spraying scenario service life time 1	1.170	1	**1.17**
PT10 Spraying scenario service life time 2	0.019	1	0.0192

For the aquatic compartment (freshwater, sediment and STP) no unacceptable risks were identified for uses of folpet in PT7 demonstrating that the risks to aquatic organisms from folpet are acceptable. For the main hydrolysis products, phtalimide and phthalic acid, risks for surface water were identified for service life (Time 2): the respective PEC/PNEC ratios are 1.01 and 1.05. However the exposure assessment was based on two worst case assumptions: 100% leaching of the applied amount during service life and treatment of roof and façade. The refinement of only one of these two assumptions (e.g. assumption of treatment of the façade only) would result in no risk for the aquatic compartment for the service life (Time 2). It is therefore considered that there are no unacceptable risks for phtalimide and phthalic acid.

Folpet PEC/PNEC rations for soil exposed to folpet following PT7 uses

Scenario	PECs (mg/kg)	PNEC (mg/kg)	PEC/PNEC
Maximum initial exposure based on **PT8** scenario (via STP - noise barrier – Time 1)	7.89 x 10-4	0.0375	0.02
Maximum exposure based on **PT8** scenarios, not taking into account degradation during the initial period (Time 1)			
adjacent to fence	2.34	0.0375	**62**
adjacent to wooden house	2.82	0.0375	**75**
adjacent to transmission pole	0.7	0.0375	**19**
adjacent to fence post	0.24	0.0375	**6.4**
Maximum exposure based on **PT8** scenarios, including degradation during the initial period (Time 1)			
adjacent to fence	0.609	0.0375	**16**
adjacent to wooden house	0.733	0.0375	**20**
adjacent to transmission pole	0.182	0.0375	**4.9**

Scenario	PECs (mg/kg)	PNEC (mg/kg)	PEC/PNEC
adjacent to fence post	0.063	0.0375	**1.7**
Maximum exposure based on **PT8** scenarios, including degradation during the longer period (Time 2)			
adjacent to fence	0.016	0.0375	0.43
adjacent to wooden house	0.0193	0.0375	0.51
adjacent to transmission pole	0.0048	0.0375	0.128
adjacent to fence post	0.0017	0.0375	0.05
Maximum initial exposure based on **PT10** scenario (via STP – spraying, city, during application)	1.28 x 10-3	0.0375	0.034
Direct exposure to soil based on **PT10** scenarios during application*			
adjacent to roof	23.8	0.0375	**634**
distant to roof	0.11	0.0375	**2.93**
adjacent to façade	20.6	0.0375	**549**
distant to façade	0.0951	0.0375	**2.53**
adjacent to house (spraying)	44.5	0.0375	**1186**
adjacent to house (brushing)	11.1	0.0375	**296**
distant to house	0.205	0.0375	**5.47**
Maximum concentration in soil adjacent to house during service life (Time 1)	0.204	0.0375	**5.44**
Maximum initial exposure based on **tonnage** distribution	1.58 x 10-4	0.0375	<0.01
PT10 Exposure of soil via the STP – City scenario - Worst Case			
PT10 Brushing scenario during application	9.9×10^{-5}	0.0375	<0.01
PT10 Brushing scenario - Service life Time 1	0.204	0.0375	**5.43**
PT10 Brushing scenario - Service life Time 2	0.003	0.0375	0.0893
PT10 Spraying scenario during application	0.013	0.0375	0.349
PT10 Spraying scenario - Service life Time 1	0.204	0.0375	**5.43**
PT10 Spraying scenario - Service life Time 2	0.003	0.0375	0.0893
PT10 Direct exposure of soil – Countryside: spraying and brushing - Worst case			
PT 10 Outdoor spraying - Application (Tier 1**)	1.188	0.0375	**31.7**
PT 10 Outdoor spraying - Application (Tier 2**)	0.131	0.0375	**3.5**
PT 10 Outdoor spraying - Service life Time 1	1.038	0.0375	**27.7**
PT 10 Outdoor spraying - Service life Time 2	0.025	0.0375	0.66
PT 10 Outdoor brushing by amateur - Application	0.198	0.0375	**5.3**
PT 10 Outdoor brushing by amateur - Service life Time 1	0.811	0.0375	**21.7**
PT 10 Outdoor brushing by amateur - Service life – Time 2	0.021	0.0375	0.56
PT 10 Outdoor brushing by professional - Application	0.119	0.0375	**3.2**
PT 10 Outdoor brushing by professional - Service life Time 1	0.781	0.0375	**20.9**
PT 10 Outdoor brushing by professional - Service life Time 2	0.020	0.0375	0.54

* For the assessment of spraying (application), the spraying scenario of the ESD for PT 10 was used

** For the assessment of spraying (application), the in-situ outdoor spraying scenario of the revised OECD ESD for PT 8 (2013) was used

Phthalimide PEC/PNEC ratios for soil exposed to folpet following PT7 uses

Scenario	PECs (mg/kg)	PNEC (mg/kg)	PEC/PNEC
Maximum initial exposure based on **PT8** scenario (via STP - noise barrier – Time 1)	8.51 x 10-4	5.0	<0.01
Maximum exposure based on **PT8** scenarios, not taking into account degradation during the initial period (Time 1)			
adjacent to fence	1.06	5.0	0.21
adjacent to wooden house	1.27	5.0	0.25
adjacent to transmission pole	0.32	5.0	0.06
adjacent to fence post	0.11	5.0	0.02
Maximum exposure based on **PT8** scenarios, including degradation during the initial period (Time 1)			
adjacent to fence	0.335	5.0	0.07
adjacent to wooden house	0.402	5.0	0.08
adjacent to transmission pole	0.100	5.0	0.02
adjacent to fence post	0.035	5.0	0.01
Maximum exposure based on **PT8** scenarios, including degradation during the longer period (Time 2)			
adjacent to fence	0.011	5.0	<0.01
adjacent to wooden house	0.0128	5.0	<0.01
adjacent to transmission pole	0.0032	5.0	<0.01
adjacent to fence post	0.0011	5.0	<0.01
Maximum initial exposure based on **PT10** scenario (via STP – spraying, city, during application)	1.38 x 10-6	5.0	<0.01
Direct exposure to soil based on **PT10** scenarios during application*			
adjacent to roof	10.7	5.0	**2.14**
distant to roof	0.0497	5.0	<0.01
adjacent to façade	9.26	5.0	**1.85**
distant to façade	0.0428	5.0	<0.01
adjacent to house (spraying)	20.0	5.0	**4**
adjacent to house (brushing)	5.0	5.0	**1**
distant to house	0.0925	5.0	0.0185
Maximum concentration in soil adjacent to house during service life (Time 1)	0.0224	5.0	<0.01
Maximum initial exposure based on **tonnage** distribution	1.73 x 10-6	5.0	<0.01
PT10 Exposure of soil via the STP – City scenario- Worst case			
PT10 Brushing scenario during application	3.68×10^{-4}	5.0	<0.01
PT10 Brushing scenario - Service life Time 1	0.0224	5.0	<0.01
PT10 Brushing scenario - Service life Time 2	1.07×10^{-5}	5.0	<0.01
PT10 Spraying scenario during application	3.68×10^{-4}	5.0	<0.01
PT10 Spraying scenario - Service life Time 1	0.0224	5.0	<0.01
PT10 Spraying scenario - Service life Time 2	1.38×10^{-4}	5.0	<0.01
PT10 Direct exposure of soil – Countryside: spraying and brushing - Worst case			
PT 10 Outdoor spraying Application (Tier 1**)	0.535	5.0	0.1
PT 10 Outdoor spraying Application (Tier 2**)	0.059	5.0	0.012
PT 10 Outdoor spraying Service life Time 1	0.622	5.0	0.12
PT 10 Outdoor spraying Service life Time 2	0.019	5.0	<0.01
PT 10 Outdoor brushing by amateur-Application	0.089	5.0	0.018
PT 10 Outdoor brushing by amateur- Service	0.478	5.0	0.096

Scenario	PECs (mg/kg)	PNEC (mg/kg)	PEC/PNEC
life Time 1			
PT 10 Outdoor brushing by amateur- Service life Time 2	0.016	5.0	<0.01
PT 10 Outdoor brushing by professional-Application	0.053	5.0	0.011
PT 10 Outdoor brushing by professional-Service life Time 1	0.459	5.0	0.092
PT 10 Outdoor brushing by professional-Service life Time 2	0.016	5.0	<0.01

* For the assessment of spraying (application), the spraying scenario of the ESD for PT 10 was used

* For the assessment of spraying (application), the in-situ outdoor spraying scenario of the revised OECD ESD for PT 8 (2013) was used

Phthalic acid PEC/PNEC ratios for soil exposed to folpet following PT7 uses

Scenario	PECs (mg/kg)	PNEC (mg/kg)	PEC/PNEC
Maximum initial exposure based on PT8 scenario (via STP - noise barrier – Time 1)	3.55 x 10-6	3.909	<0.01
Maximum exposure based on PT8 scenarios, not taking into account degradation during the initial period (Time 1)			
adjacent to fence	1.03	3.909	0.26
adjacent to wooden house	1.24	3.909	0.32
adjacent to transmission pole	0.31	3.909	0.08
adjacent to fence post	0.11	3.909	0.03
Maximum exposure based on PT8 scenarios, including degradation during the initial period (Time 1)			
adjacent to fence	0.106	3.909	0.03
adjacent to wooden house	0.127	3.909	0.03
adjacent to transmission pole	0.032	3.909	<0.01
adjacent to fence post	0.011	3.909	<0.01
Maximum exposure based on PT8 scenarios, including degradation during the longer period (Time 2)			
adjacent to fence	0.002	3.909	<0.01
adjacent to wooden house	0.00058	3.909	<0.01
adjacent to transmission pole	0.003	3.909	<0.01
adjacent to fence post	0.0002	3.909	<0.01
Maximum initial exposure based on PT10 scenario (via STP – spraying, city, during application)	9.17 x 10-4	3.909	<0.01
Direct exposure to soil based on PT10 scenarios during application*			
adjacent to roof	10.4	3.909	**2.66**
distant to roof	0.048	3.909	0.01
adjacent to façade	8.95	3.909	2.29
distant to façade	0.0414	3.909	<0.01
adjacent to house (spraying)	19.3	3.909	**4.94**
adjacent to house (brushing)	4.84	3.909	**1.24**
distant to house	0.0894	3.909	0.03
Maximum concentration in soil adjacent to house during service life(Time 1)	9.17 x 10-4	3.909	<0.01
Maximum initial exposure based on tonnage distribution	7.17 x 10-7	3.909	<0.01
PT10 Exposure of soil via the STP – City scenario - Worst case			
PT10 Brushing scenario during application	1.51E-05	3.909	<0.01
PT10 Brushing scenario service life time 1	9.17E-04	3.909	<0.01
PT10 Brushing scenario service life time 2	4.40E-07	3.909	<0.01
PT10 Spraying scenario during application	1.51E-05	3.909	<0.01
PT10 Spraying scenario service life time 1	9.17E-04	3.909	<0.01
PT10 Spraying scenario service life time 2	5.71E-06	3.909	<0.01
PT10 Direct exposure of soil – Countryside: spraying and brushing - Worst case			
PT 10 Outdoor spraying Application (Tier 1)**	0.517	3.909	0.13
PT 10 Outdoor spraying Application (Tier 2)**	0.059	3.909	0.015
PT 10 Outdoor spraying - Service life Time 1	0.179	3.909	0.05

Scenario	PECs (mg/kg)	PNEC (mg/kg)	PEC/PNEC
PT 10 Outdoor spraying -Service life Time 2	0.019	3.909	<0.01
PT 10 Outdoor brushing by amateur - Application	0.086	3.909	0.02
PT 10 Outdoor brushing by amateur- Service life Time 1	0.147	3.909	0.04
PT 10 Outdoor brushing by amateur- Service life Time 2	0.016	3.909	<0.01
PT10 Outdoor brushing by professional - Application PT 10 Outdoor brushing by professional- Service life – Time 1	0.143	3.909	0.04
PT 10 Outdoor brushing by professional Service life – Time 2	0.016	3.909	<0.01

* For the assessment of spraying (application), the spraying scenario of the ESD for PT 10 was used

** For the assessment of spraying (application), the in-situ outdoor spraying scenario of the revised OECD ESD for PT 8 (2013) was used

PEC/PNEC ratios for folpet and its main hydrolysis products phthalimide and phthalic acid were calculated for application and service life using different ESDs.

When assessing the **application phase** for **folpet**, unacceptable risk was found when direct exposure to soil occurs (spraying and brushing in the countryside). When assessing the exposure to soil via sewage sludge application to agricultural land (city scenario) the PEC/PNEC ratios were all below 1 and therefore acceptable.

When assessing the **service life**, degradation in soil was taken into account. Considering exposure to soil via sewage sludge application (city scenario) unacceptable risk (5.43) was found at Time 1, nevertheless PEC/PNEC ratios were below 0.1 when calculating Time 2, therefore acceptable risk to soil organisms was found in a city scenario. Considering direct release to soil (spraying and brushing in the countryside), unacceptable risk to soil was found for Time 1 but acceptable risk was found for Time 2 for both types of application (brushing and spraying).

Folpet hydrolyses quickly to the hydrolysis products phthalimide and phthalic acid, therefore the actual likelihood of exposure to folpet in soil is limited and the risk assessment for the metabolites is potentially more relevant. Moreover, folpet has a long history of use in the plant protection sector, with patterns of application that result in direct exposure of terrestrial biota. No instances of adverse effects on terrestrial organisms have been reported, in spite of direct exposure to the active substance at application rates and soil concentrations significantly higher than those predicted to arise in localised patches of soil following the proposed biocidal uses of folpet.

PECs for **phthalimide** and **phthalic acid** were calculated using the same scenarios as for folpet. PEC/PNEC ratios below 1 were found for both metabolites during application and during service life at Time 1 and Time 2 (for both application types spraying and brushing) and for country side and city scenarios, indicating a safe uses.

As a conclusion, unacceptable risk to soil organisms was found for areas immediately adjacent to the treated surface when direct exposure to folpet takes place (painting and brushing by professionals and amateurs in the countryside). However, the actual likelihood of folpet soil exposure is very low because of rapid hydrolysis. Folpet will have degraded to the hydrolysis products phthalimide and phthalic acid prior to any soil exposure and therefore risk assessment for these metabolites is potentially more relevant

Nevertheless, since a risk to the soil environment is indicated measures shall be taken to protect the soil to prevent losses and minimise emissions to the environment

Groundwater
Estimations of PEC groundwater for folpet, phthalimide and phthalic acid were conducted in a tiered approach; firstly soil porewater calculations were conducted followed by simulations using the FOCUS methodology and the PEARL model. The results are summarised in the following tables.

Summary of maximum predicted concentration in soil porewater

Parameter	Folpet	Phthalimide	Phthalamic acid	Phthalic acid
Resulting soil pore-water concentration, PEClocalsoil, porew (µg/L).	0.039	0.018	0.114	0.015

FOCUS predicted groundwater concentrations of folpet and associated metabolites via sewage sludge applications to land following biocidal use (PT7)

Scenario	80th percentile annual average concentration (µg/L)			
	folpet	phthalimide	phthalamic acid	phthalic acid
Land applications (1 Feb, 1 May and 1 Sep) for PT 6, 7 and 9				
Châteaudun (C)	< 0.001	< 0.001	< 0.001	< 0.001
Hamburg (H)	< 0.001	< 0.001	< 0.001	< 0.001
Jokioinen (J)	< 0.001	< 0.001	< 0.001	< 0.001
Kremsmünster (K)	< 0.001	< 0.001	< 0.001	< 0.001
Okehampton (N)	< 0.001	< 0.001	< 0.001	< 0.001
Piacenza (P)	< 0.001	< 0.001	< 0.001	< 0.001
Porto (O)	< 0.001	< 0.001	< 0.001	< 0.001
Sevilla (S)	< 0.001	< 0.001	< 0.001	< 0.001
Thiva (T)	< 0.001	< 0.001	< 0.001	< 0.001

Using the FOCUS methodology, the 80th percentile PECgw values of the active substance folpet and associated metabolites in groundwater were generated assuming repeated annual applications at the maximum seasonal treatment rate. Annual average concentrations were calculated as the cumulative annual chemical flux divided by the cumulative annual water recharge volume at 1 m depth. A direct soil surface application type was used for PEARL calculations, as worst case condition. The predicted concentration is a conservative estimate of what may actually be expected in groundwater used for drinking water as soil pore water at one-meter depth is not a likely source of drinking water.

In the reasonable worst-case scenarios, the annual average concentration of the active substance folpet and associated metabolites in soil pore water at one-meter depth was much less than 0.1 µg/L. The results from this modelling study indicated that the leaching potential of the active substance folpet and associated metabolites is very low (80th percentile PECgw <0.001 µg/L) under all FOCUS leaching scenarios.

The groundwater assessment is based on a soil application rate of 3.075 kg/ha which is equivalent to a soil concentration of 4.1 mg/kg, assuming distribution to a depth of 5 cm

and a soil density of 1.5 g/cm^3. The range of predicted soil concentrations from EUSES modelling are 0.0788 to 14.7 mg/kg in scenarios considering exposure around treated buildings. Based on the FOCUS modelling presented, soil concentrations in the range predicted by EUSES are not expected to pose a risk to groundwater.

A groundwater assessment was also conducted according to the revised PT8 OECD emission scenario document considering 10 leaching events to soil per year at a rate of 0.02 kg/ha for folpet, 0.009 kg/ha for phthalimide, and 0.009 kg/ha for phthalic acid.The resulting groundwater concentrations are presented in the table below.

Predicted groundwater concentrations of folpet and associated metabolites from releases to soil during service life of PT7 products.

Scenario	80th percentile annual average concentration (µg/L)			
	folpet	phthalimide	phthalamic acid	phthalic acid
Châteaudun (C)	< 0.001	< 0.001	< 0.001	< 0.001
Hamburg (H)	< 0.001	< 0.001	< 0.001	< 0.001
Jokioinen (J)	< 0.001	< 0.001	< 0.001	< 0.001
Kremsmünster (K)	< 0.001	< 0.001	< 0.001	< 0.001
Okehampton (N)	< 0.001	< 0.001	< 0.001	< 0.001
Piacenza (P)	< 0.001	< 0.001	< 0.001	< 0.001
Porto (O)	< 0.001	< 0.001	< 0.001	< 0.001
Sevilla (S)	< 0.001	< 0.001	< 0.001	< 0.001
Thiva (T)	< 0.001	< 0.001	< 0.001	< 0.001

2.2.3. Assessment of endocrine disruptor properties

Based on the available data and repeated dose toxicity studies performed with folpet that do not indicate effects on the reproductive tract or other hormone-sensitive tissues, there is no evidence to raise endocrine related concern associated with folpet or its metabolites.

2.3.Overall conclusions

a) Presentation of the active substance and representative biocidal product including classification of the active substance

Trade name	**Folpet**	
Manufacturer´s development code number(s)	-	
Ingredient of preparation	**Function**	**Content %**
Folpet	Active substance	not less than 94% (w/w) *
Impurities	The biocidal product for PT7 film preservative use is folpet technical. The technical material is added directly during the formulation of paint, mastic, sealer, filler and adhesive products (the treated article). The composition of the folpet technical is confidential to Makhteshim Chemical Works Ltd. is presented in the confidential attachment. Full details of the impurities and inert components are also presented in the confidential attachment.	
Physical state of preparation	Folpet technical is a solid in the form of powder/crystals. It is not formulated as a preparation for biocide use.	
Nature of preparation		

* The minimum purity of folpet is proposed in compliance with that agreed for Annex I inclusion under Directive 91/414/EEC.

The biocidal product for PT7 film preservative use is folpet technical. The current classification and labelling for folpet according to Directive 67/548/EEC is as follows:

Hazard(s)	Xn N	Harmful Dangerous for the environment
Risk Phrase(s)	R20 R36 R40 R43 R50	Harmful by inhalation Irritating to eyes Limited evidence of a carcinogenic effect May cause sensitisation by skin contact Very toxic to aquatic organisms
Safety Phrase(s)	S2 S36/37 S46 S61	Keep out of the reach of children Wear suitable protective clothing and gloves If swallowed, seek medical advice immediately and show the container or label Avoid release into the environment. Refer to special instructions/Safety data sheets
Classification according to Regulation (EC) No 1272/2008		
Hazard statement codes	GHS07 GHS08 GHS09 Warning	
Hazard Class, category code and hazard statement	Acute Tox 4 Eye Irritation Cat 2 Skin Sensitisation 1 Carc. Cat. 2 Aquatic Acute 1	H332 Harmful if inhaled H319 Causes serious eye irritation H317 May cause an allergic skin reaction H351 Suspected of causing cancer H400 Very toxic to aquatic life M=10

On basis of information presented in the dossier, it is proposed not to change the current classification and labelling.

b) Intended use, target species and effectiveness: containing a description of the use(s) evaluated in the assessment report

Folpet is a fungicide and bactericide used as a film preservative (PT 7) for use in products including paints, mastics, sealants, fillers and adhesives showing a preservative effect (e.g. wallpaper paste). Products containing folpet may be used by professionals (decorators and builders) and non-professionals. Typical application is manual (by brush, roller or spray apparatus). Folpet is used to control fungal species (*Candida albicans*)

The active substance, folpet, is applied once to the treated article during manufacture. The active substance, folpet, is not used directly by users.

Use assumptions based on the available guidance are as follows:

- Professional user: brush and roller application, 360 mins per day. Daily use.
- Professional user: spray application, 360 minutes per day.
- Non-professional user: brush and roller application, 4 hours per day, 2 to 5 days per year.

The mechanism of the fungicidal action of folpet is outlined as follows. Folpet enters the conidia of the target organisms, where its toxicity is attributed to the activity of the thrichloromethylthio (SCCl3, TCM) group, which inhibits oxidative enzymes, carboxylases and enzymes involved in phosphate metabolism and citrate synthesis. Folpet reacts with the sulphhydryl groups of the nuclear proteins, which causes the inhibition of cell division. Spore germination is hindered as a result. The reaction of folpet and the reaction of thiophosgene, one of its decomposition products, with thiols and other groupings may be a

means of metabolic inhibition. Thiophosgene can react with thiol groups to form thiocarbonates or with amino acids to form thiourea derivatives. Since folpet is a general thiol reactant, the mechanism of action against target organisms is non-specific and is not the result of a single interaction at a specific site. Coenzyme A is an important site of action. Since Coenzyme A is a very important thiol in cell metabolism, its inactivation affects many enzyme systems. Thiophosgene functions as a toxicophore of folpet in its effectiveness against target organisms, but in combination with the parent active substance and not as the sole active principle.

Although folpet is unstable in aqueous solution, the rate of its hydrolysis is slower than the speed at which it reacts with thiols. The balance between the reactivity of the TCM moiety of folpet and the stability of the N-S bond that links the TCM group to its imide ring is critical in determining folpet's effectiveness as a fungicide. Analogous structures with very stable bonds are ineffectual fungicides, whilst structural analogues that have N-S bonds that are too easily broken cleave spontaneously.

Over more than 50 years of use, folpet has demonstrated its efficacy as a valuable fungicide and bactericide for a wide spectrum of diseases used in many products as biocide. Being a protectant non-systemic fungicide, folpet is widely used in a large range of fungicidal mixtures or combinations, specifically designed for improving efficacy and in prevention of resistance to the systemic products.

In laboratory testing 0.2% Folpet demonstrated good yeasticidal activity against *C. albicans* and basic innate activity was demonstrated against other organisms. Full efficacy will be proven at Product Authorisation stage. In addition, good efficacy has been demonstrated against a range of target species in polymeric material containing folpet.

c) Risk characterisation for human health

The endpoints for folpet and information relating to its toxicological properties and classification are provided in Appendix 1 Listing of endpoints, Chapter 3. This information is used to set the Acceptable Exposure Levels (AEL) value that was determined to be 0.1 mg/kg bw/d (as determined by the EU review of folpet under Directive 91/414/EEC using this data set). A short-term AEL value of 0.2 mg/kg bw is also derived.

The estimated exposure is compared to the systemic AEL for each relevant component.

Summary table: scenarios			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
1.	Spraying	360 minutes, daily	Professional
2.	Brush and roller	360 minutes/day	Professional
3.	Brush and roller	4 hours/day; 2-5 days per year	Non-professional

Conclusion of risk characterisation for industrial user

The potential areas of exposure during manufacturing and /or formulation – inhalation, dermal exposure and oral ingestion – have been minimised by the use of automated processes and engineering controls integral to the processes and further reduced by the

requirements to wear suitable protective equipment (including gloves, protective clothing, eye and dust protection) whenever exposure to the active ingredient or other ingredients is likely.

Therefore, exposure of manufacturing and formulation workers is rigorously controlled and no further detailed assessment is necessary.

Conclusion of risk characterisation for professional user

Scenario	**Relevant reference value**[2]	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
Brush and roller application: Model 1 No gloves	medium-term AEL = 0.1 mg/kg bw/d	0.224	224	No
	Acute exposure: short-term AEL = 0.2 mg/kg bw/d		112	No
Brush and roller application: Model 1 Gloves only	medium-term AEL = 0.1 mg/kg bw/d	0.112	112	No
	Acute exposure: short-term AEL = 0.2 mg/kg bw/d		56	Yes
Brush and roller application: Model 1 Gloves and coverall	medium-term AEL = 0.1 mg/kg bw/d	0.023	23	Yes
	Acute exposure: short-term AEL = 0.2 mg/kg bw/d		12	Yes
Brush/roller (PHED) No gloves	medium-term AEL = 0.1 mg/kg bw/d	0.014	14	Yes
	Acute exposure: short-term AEL = 0.2 mg/kg bw/d		7	Yes
Brush/roller (PHED) Gloves	medium-term AEL = 0.1 mg/kg bw/d	0.002	2	Yes
	Acute exposure: short-term AEL = 0.2 mg/kg bw/d		1	Yes
Brush washing No gloves	medium-term AEL = 0.1 mg/kg bw/d	0.00057	0.6	Yes
	Acute exposure: short-term AEL = 0.2 mg/kg bw/d		0.3	Yes
Brush washing Gloves	medium-term AEL = 0.1 mg/kg bw/d	0.00006	0.06	Yes
	Acute exposure: short-term AEL = 0.2 mg/kg bw/d		0.02	Yes
Paint spraying Gloves only	medium-term AEL = 0.1 mg/kg bw/d	0.156	156	No
	Acute exposure:		78	Yes

Scenario	Relevant reference value[2]	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
	short-term AEL = 0.2 mg/kg bw/d			
Paint spraying Gloves and coverall	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.021	21 11	Yes Yes
Airless spraying (PHED) No gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.0005	0.5 0.3	Yes Yes
Airless spraying (PHED) Gloves only	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.0004	0.4 0.2	Yes Yes
Cleaning spray equipment No gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.0000072	0.007 0.004	Yes Yes

Folpet is not classified as a skin irritant based on the results of a skin irritation study, according to CLH Folpet is classified as skin sensitizer Cat 1. The levels of folpet achieved in the end-use product of 2 g/kg (0.2 %) are much lower than the concentrations eliciting positive responses in the Maximisation study. Considering the CLP sub-categories (Skin Sens. 1A and 1B) , folpet would not be classified as a strong sensitiser based on the results of the maximisation study and is therefore considered to have low to moderate potency as a sensitiser.. Additionally, the concentrations of folpet are below the threshold for classification of the product according to Directive 99/45/EEC and though the a.s. is classified the end-use product (paint) would not been classified as a skin sensitiser.

While folpet is not classified as a skin irritant based on the results of a skin irritation study, repeated dermal application in a 28-day study resulted in significant local effects in all groups (0.5 mg/ml; 1 mg/kg bw/d and above). The findings of this study, in which folpet was repeatedly applied for 6 hour periods in mineral oil under occlusive conditions are not considered to be of direct relevance to the human risk assessment. Ready-to-use products typically contain folpet at levels of 0.2%; risk assessment for professional workers requires the use of gloves. It is therefore considered very unlikely that the normal use of folpet products would result in a level of dermal contamination resulting in local irritation.

Moreover, Folpet was officially classified at the 28th ATP (Commission directive 2001/59/EC) and no classification for skin irritation was assigned, based on the 28 day study.

Conclusion of risk characterisation for non-professional user

Scenario	**Relevant reference value**[2]	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
Brush and roller application (Painting Model 1) No gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.15	150 75	No Yes
Brush and roller application (Painting Model 1) Gloves only	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.075	75 38	Yes Yes
Washing brushes No gloves	medium-term AEL =0.1 mg/kg bw/d	0.00057	0.57	Yes
Washing brushes Gloves	medium-term AEL =0.1 mg/kg bw/d	0.00003	0.03	Yes

Conclusion of risk characterisation for indirect exposure

Scenario	**Relevant reference value**[2]	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
Laundering contaminated overalls	short-term AEL = 0.2 mg/kg bw/d	0.016	8	Yes
Dermal contact with wet product by child	short-term AEL = 0.2 mg/kg bw/d	0.17	85	Yes
Oral ingestion child	short-term AEL = 0.2 mg/kg bw/d	0.041	20	Yes
Inhalation exposure child	short-term AEL = 0.2 mg/kg bw/d	0.0008	0.4	Yes
Dermal contact with surface bloom on preserved mastic	short-term AEL = 0.2 mg/kg bw/d	0.025	12.5	Yes

Conclusion on aggregated exposure

Professional and non-professional users are potentially at risk of exposure from several sources during or after use of products containing folpet. However, the exposure estimates are based on daily work rates and, therefore, the combination of any individual tasks is not applicable. The application (brush and roller) and post application (cleaning of brushes) of

in-can preserved paints could potentially occur on the same day and therefore, combined exposure was considered.

Combined exposure for the professional user

Scenario	**Relevant reference value**	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
Brush and roller application: Model 1 and Brush washing No gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.22475	225 112	No No
Brush and roller application: Model 1 and Brush washing Gloves only	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.11206	112 56	No Yes
Brush and roller application: Model 1 Gloves and coverall and Brush washing Gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.02306	23 12	Yes Yes
Brush/roller (PHED) and Brush washing No gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.01475	15 7	Yes Yes
Brush/roller (PHED) and Brush washing Gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.00206	2 1	Yes Yes
Paint spraying Gloves only And Cleaning spray equipment No Gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.1560072	156 78	No Yes

Scenario	**Relevant reference value**	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
Paint spraying Gloves and coverall And Cleaning spray equipment No Gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.0210072	21 11	Yes Yes
Airless spraying (PHED) And Cleaning spray equipment No gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.0005072	0.5 0.3	Yes Yes
Airless spraying (PHED) Gloves only And Cleaning spray equipment No Gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.0004072	0.4 0.2	Yes Yes

Combined exposure for the non-professional user

Scenario	**Relevant reference value**	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
Brush and roller application (Painting Model 1) And Washing brushes No gloves	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.15075	151 75	No Yes
Brush and roller application (Painting Model 1) And Washing brushes Gloves only	medium-term AEL = 0.1 mg/kg bw/d Acute exposure: short-term AEL = 0.2 mg/kg bw/d	0.07503	75 38	Yes Yes

The risk of acute or chronic exposure to the relevant components for all non-users is considered to be negligible.

Overall conclusion on human health risk characterization

Exposure levels resulting from the intended professional uses of products containing the film preservative folpet on a daily basis are therefore estimated to be below the AEL when PPE such as gloves are worn. Exposure levels resulting from the intended uses for non-professional users during use of paint containing the preservative folpet on a daily basis are below the AEL when based on worst-case default values. Indirect acute exposure levels resulting from the intended use of folpet as a film preservative are therefore estimated to be below the acute AEL when based on worst-case default values.

d) Risk characterisation for environment

For the **aquatic compartment** (freshwater, sediment and STP) no unacceptable risks were identified for uses of folpet as a PT6 in-can preservative demonstrating that the risks to aquatic organisms from folpet are acceptable. For the main hydrolysis products, phtalimide and phthalic acid, risks (PEC/PNEC ratios slightly in excess of 1) for surface water were identified for service life. However the exposure assessment was based on worst case assumptions.The refinement of these assumptions would result in no risk for the aquatic compartment for the service life (Time 2). It is therefore considered that there are no unacceptable risks for phtalimide and phthalic acid.

For the **terrestrial compartment** (soil), when assessing the application phase for folpet, unacceptable risk was found when direct exposure to soil occurs (spraying and brushing in the countryside). When assessing the exposure to soil via sewage sludge application to agricultural land (city scenario) the PEC/PNEC ratios were all below 1 and therefore acceptable.

When assessing the service life of the product, degradation in soil was taken into account. Considering exposure to soil via sewage sludge application (city scenario) unacceptable risk was found at Time 1, nevertheless PEC/PNEC ratios were below 0.1 when calculating Time 2, therefore acceptable risk to soil organisms was found in a city scenario. Considering direct release to soil (spraying and brushing in the countryside), unacceptable risk to soil was found for Time 1 but acceptable risk was found for Time 2 for both types of application (brushing and spraying).

PECs for phthalimide and phthalic acid were calculated using the same scenarios as for folpet. PEC/PNEC ratios below 1 were found for both metabolites during application and during service life at Time 1 and Time 2 (for both application types spraying and brushing) and for country side and city scenarios, indicating a safe uses.

As a conclusion, unacceptable risk to soil organisms was found for areas immediately adjacent to the treated surface when direct exposure to folpet takes place (painting and brushing by professionals and amateurs in the countryside). However, the actual likelihood of folpet soil exposure is very low because of rapid hydrolysis. Folpet will have degraded to the hydrolysis products phthalimide and phthalic acid prior to any soil exposure and therefore risk assessment for these metabolites is potentially more relevant. Nevertheless, since a risk to the soil environment is indicated by the modelled calculations for folpet and to a lesser extent the more relevant hydrolysis products, phthalimide and phthalic acid measures shall be taken to protect the soil to prevent losses and minimise emissions to the environment.

Regarding the **groundwater**, no unacceptable risks were identified with the scenario assessed (revised PT8 OECD emission scenario and FOCUS scenario).

e) Substitution and exclusion criteria

Folpet is not classified for human health hazard as a Category 1A/1B carcinogen, mutagen or reproductive toxicant. Folpet is not considered to have endocrine disrupting properties and does not meet the criteria as a PBT substance or a vPvB substance. Folpet therefore does not fulfil the exclusion criteria for active substances set down in Article 5(1) of Regulation 528/2012.

Folpet does not fulfil any of the exclusion criteria according to Article 5(1) of the Regualtion 528/2012. Fopet is not classified as a resoiratory sensitiser, does not fulfil any PBT criteria and presents a negligible risk to groundwater for the uses supported under PT7. The acute AEL (0.1 mg/kg bw/day) and chronic AEL (0.2 mg/kg bw/day) values for folpet are not considered to be low in the context of PT7 use. Folpet therefore does not fulfil the substitution criteria for active substances set down in Article 10(1) of Regulation 528/2012.

As exclusion criteris or substitution criteris are not fulfilled, approval of the active substance folpet should be granted for an initial period of 10 years in accordance with Article 4 of Regulation 528/2012.

f) Overall conclusion evaluation including need for risk management measures

Since a risk to the soil environment is indicated by the modelled calculations for folpet and to a lesser extent the more relevant hydrolysis products, phthalimide and phthalic acid, measures shall be taken to protect the soil to prevent losses and minimise emissions to the environment.

List of endpoints

The most important endpoints, as identified during the evaluation process, are listed in Appendix I.

The following additional data will be provided at the Product Authorisation stage:

- efficacy data;
- a list of additional scenarios to be assessed at the product authorisation stage: e.g. additional consumption scenarios e.g. the bridge scenario [direct release to water], roof membrane and shower scenario to address specific uses with leaching to the environment.

Appendix I: List of endpoints

Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

Active substance (ISO Common Name)	Folpet
Product-type	PT 7

Identity

Chemical name (IUPAC)	N-(trichloromethylthio) phthalimide N-(trichloromethanesulfenyl)phthalimide
Chemical name (CA)	2-[(trichloromethyl)thio]-1H-isoindole-1,3(2H)-dione
CAS No	133-07-3
EC No	205-088-6
Other substance No.	CIPAC 75
Minimum purity of the active substance as manufactured (g/kg or g/l)	940 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Identity of impurities is presented in the confidential attachment.
Molecular formula	$C_9H_4Cl_3NO_2S$
Molecular mass	296.6
Structural formula	

Physical and chemical properties

Melting point (state purity)	179 - 180°C (99.6% purity)
Boiling point (state purity)	Not relevant - test substance is a solid
Temperature of decomposition	Not required as melting point has been determined.
Appearance (state purity)	White solid crystals (98.8% purity)
Relative density (state purity)	1.72 (99.6% purity)
Surface tension	Not required because the water solubility of the active substance is less than 1.0 mg/L.
Vapour pressure (in Pa, state temperature)	2.1 x 10^{-5} Pa (25°C) 9.7 x 10^{-5} Pa (35°C) 4.5 x 10^{-4} Pa (45°C)
Henry's law constant (Pa m^3 mol^{-1})	8 x 10-3 Pa.m3.mol-1 at 25°C
Solubility in water (g/l or mg/l, state temperature)	pH__5____: Not determined
	pH__9____: Not determined
	pH 6.7: 0.80 mg/L (max., 25°C)

	pH 6.7: 0.50 mg/L (mean, 15°C)
Solubility in organic solvents (in g/l or mg/l, state temperature)	Acetone : 34 g/L (25°C)
	n-octanol: 1.4 g/L (25°C)
	Methanol: 3.1 g/L (25°C)
	Toluene: 26.3 g/L (25°C)
	carbon tetrachloride: 6 g/L (25°C)
	Acetonitrile: 19 g/L (25°C)
	Heptanes: 0.05 g/L(25°C)
Stability in organic solvents used in biocidal products including relevant breakdown products	Not applicable because the active substance as manufactured does not include an organic solvent and is not formulated in organic solution in the biocidal product.
Partition coefficient (log P_{OW}) (state temperature)	pH___5___: Not determined
	pH___9___: Not determined
	pH_____: 3.017
Hydrolytic stability (DT_{50}) (state pH and temperature)	Folpet
	2.6 hours (pH 5; 25°C) 1.1 hours (pH 7; 25°C) 67 seconds (pH 9; 25°C and 40°C)
	pH4 and 12°C = 17.1 hours (mean) pH5 and 12°C = 8.7 hours pH7 and 12°C = 2.7 hours (mean) pH9 and 12°C = 0.1 hours
Dissociation constant	Folpet is unlikely to dissociate in water because it does not contain a proton that will dissociate at environmentally relevant pHs. Therefore, it is considered unnecessary to determine the pKa.
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	The molar extinction coefficient (M-1 cm-1): 47100, 7900, 1780, 1720 at 223, 236, 295, 300 nm (purified water:methanol 1:9 v/v) 52600, 8410, 1770, 1720 at 223, 237, 296, 301 nm (aqueous hydrochloric acid: methanol 1:9) 19900, 11300, 7410, 1810, 1650, 1320 at 225, 238, 247, 280, 289, 301 nm (aqueous sodium hydroxide: methanol 24:1)
Photostability (DT_{50}) (aqueous, sunlight, state pH)	Photolysis either does not occur or is very slow relative to hydrolysis.
Quantum yield of direct phototransformation in water at > 290 nm	Due to the rapid chemical hydrolysis of folpet the quantum yield is impossible to measure experimentally – No data submitted.
Flammability	Not classified as flammable.
Explosive properties	Non-explosive.

Classification and proposed labelling

with regard to physical/chemical data	None
with regard to toxicological data	Xn, R20, R36, R40, R43 Carc (H351); Acute Tox 4 (H332); Eye Irrit 2 (H319); Skin Sens 1 (H317)
with regard to fate and behaviour data	None
with regard to ecotoxicological data	N, R50 Aquatic Acute 1 (H400)

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	Folpet technical material is dissolved in an acetonitrile solution containing the internal standard, propyl paraben. The sample is sonicated and filtered prior to determination by reverse-phase HPLC/UV. HPLC/UV determination is carried out at a wavelength of 254 nm using a C18 column and an acetonitrile/water/trifluoroacetic acid mobile phase.
Impurities in technical active substance (principle of method)	See confidential attachment.

Analytical methods for residues

Soil (principle of method and LOQ)	1. Folpet and phthalimide are extracted by shaking with aqueous acetonitrile and residues are partitioned into dichloromethane. The extract is purified by C18 solid phase extraction cartridge prior to determination by capillary GC/ECD. The LOQ is 0.05 mg/kg for folpet and phthalimide. 2. A confirmatory procedure is presented for the determination of folpet residues in soil. Residues are extracted by shaking with aqueous acetonitrile. The extract is saturated with sodium chloride and the organic phase is evaporated to dryness prior to reconstitution in hexane/ethyl acetate. The extracts are purified by solid phase extraction on activated carbon. Determination of folpet is by capillary GC/MS with selected ion monitoring (five ions monitored). The limitof quantification is 0.05 mg folpet/kg.
Air (principle of method and LOQ)	A measured volume of air is drawn through a filter paper and two activated silica gel tubes arranged in series by an air sampling pump. The filter paper and the front silica gel adsorbent are extracted by shaking with acetonitrile. The silica gel from the back tube is analysed separately to determine breakthrough. Determination of folpet is by reverse-phase HPLC/UV with a photodiode array detector. The LOQ is 21µg/m^3 in 480 L of air.
Water (principle of method and LOQ)	Folpet is extracted from water by shaking with dichloromethane. Determination is by reverse-phase HPLC/UV with a photodiode array detector. Additionally, a GC/ECD determination method is provided. The GC/ECD method was found not to be adequately repeatable but may be usefully employed for confirmatory purposes. The LOQ is 0.02 µg/L. Folpet is extracted from pond water with toluene prior to quantification of folpet by gas chromatography with mass spectrometric detection (GC-MS). Analysis of phthalimide, phthalamic acid, phthalic acid, 2-cyanobenzoic acid and benzamide in pond water samples is by extraction with dichloromethane prior to quantification of phthalimide by (GC-MS). The

remaining aqueous phase, post extraction, is quantified directly by liquid chromatography with tandem mass spectrometric detection (LC-MS/MS) for the determination of phthalamic acid, phthalic acid, 2-cyanobenzoic acid and benzamide.
Analysis of folpet, phthalimide, phthalamic acid, phthalic acid, 2-cyanobenzoic acid and benzamide in pond sediment samples comprises of extraction with toluene and cleanup using ENVI-Carb solid phase extraction prior to quantification of folpet and phthalimide by (GC-MS). The remaining aqueous phase, post extraction, is quantified directly by liquid chromatography with tandem mass spectrometric detection (LC-MS/MS) for the determination of phthalamic acid, phthalic acid, 2-cyanobenzoic acid and benzamide.

The LOQs are as follows:

Analyte	**Matrix**	**LOQ**
Folpet	Water Sediment	1 µg/L 5 ng/g
Phthalimide	Water Sediment	0.5 ug/L 20 ng/g
Phthalamic acid	Water Sediment	2.5 ug/L 20 ng/g
Phthalic acid	Water Sediment	2.5 ug/L 20 ng/g
2-Cyanobenzoic acid	Water Sediment	0.5 ug/L 5 ng/g
Benzamide	Water Sediment	0.5 ug/L 5 ng/g

Folpet is extracted from drinking water by liquid:liquid partition with toluene. For extraction of phthalimide liquid:liquid partition with dichloromethane is used. Quantitation of both folpet and phthalimide is by gas chromatography with mass spectrometric detection (GC-MS). Quantitation of phthalic acid in drinking water is by liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). Phthalamic acid and benzamide are acidified and quantitation is by liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). For 2-cyanobenzoic acid solid phase extraction (SPE) is used with NH2 cartridges followed by quantitation by liquid chromatography with tandem mass spectrometric detection (LC-MS/MS).

The LOQs are 0.2 ng/mL for folpet and phthalimide, 1 ng/mL for 2-cyanobenzoic acid and 0.05 ng/mL for benzamide (= 0. 05 ug/L in sample matrix for these analytes). The limit of determination of the analytical system for phthalic acid and phthalamic acid was 1 ng/mL (= 1 ug/L in sample matrix for these analytes).

Body fluids and tissues (principle of method and LOQ)	Folpet is not classified as highly toxic or toxic to humans. Therefore, methods for the determination of folpet in body fluids and tissues are not required.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not relevant because the product or treated materials will not come into contact with food or feedstuffs.
Food/feed of animal origin (principle of method	Not relevant because the product or treated materials will

and LOQ for methods for monitoring purposes)	not come into contact with food or feedstuffs.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Folpet is considered to be completely and rapidly absorbed following oral administration (>80%).
Rate and extent of dermal absorption for the active substance:	10% (default; EFSA-agreed)
Rate and extent of dermal absorption for the representative product(s):	Human/rat in vitro and rat in vivo: <10% for aqueous dilute formulations containing similar or greater concentrations of folpet to paints (actual range 4.22 – 9.19%). No data are available for folpet in formulation as an in-can preservative, but many of the uses are anticipated to be either in aqueous media, or aqueous emulsions at high dilutions, such that aqueous solutions of a WDG and an SC plant protection formulation are considered acceptable substitutes. Comparison of in vivo rat and in vitro rat and human data for Folpan 50 SC and Folpan 80 WDG showed that dermal penetration of the undiluted formulations as supplied was 0.07% and 0.95%, respectively. At an in-use spray concentration of 1.25 g a.s./L, dermal absorption was 6.54% and 9.19% absorption for Folpan 50 SC and Folpan 80 WDG, respectively. At an in-use spray concentration of 7.5 g a.s./L, dermal absorption was 6.24% and 4.22% for Folpan 50 SC and Folpan 80 WDG, respectively. Based on the range of values reported, a conservative dermal absorption value of 10% is therefore used for the purposes of risk assessment of biocidal products typically containing folpet at a level of 0.2%.
Distribution:	In rats, the radioactivity was distributed within the body of the treated animals at generally low concentration levels. This activity, however, was not associated with parent compound, as folpet degrades in whole blood with a half-life of 4.9 seconds. Tissue residues negligible because of rapid excretion.
Potential for accumulation:	The low amount of residues and the rapid excretion led to the conclusion that no accumulation or relevant concentration occurred in the rat.
Rate and extent of excretion:	In rats, excretion predominantly via urine was essentially completed 24 hours after dosing by oral administration. The systemic half-life of [14C] was no greater than approximately 12 hours.
Toxicologically significant metabolite(s)	Folpet is highly unstable, with a half-life of 4.9 seconds in whole blood. The most significant pathway is the potential for the trichloromethylthio side-chain to degrade, by hydrolysis, to thiophosgene, which is highly reactive. Thiophosgene is also unstable in whole blood, with a half-life of 0.6 seconds. Removal of the side-chain by hydrolysis or by detoxification mechanisms gives phthalimide, which is

	capable of hydroxylation in the aromatic ring (demonstrated at the 3- and 4- positions). Phthalimide is further metabolised to phthalamic acid, which in turn may be converted to phthalic acid and phthalic anhydride. It has been postulated that the hydroxylated phthalimides may also be metabolised to the corresponding phthalamic acids and phthalic acids. Derivatives of phthalimide are excreted predominantly in the urine mostly within 24 hours of folpet administration, and show no potential for accumulation.

Acute toxicity

Rat LD_{50} oral	> 2,000 mg/kg bw	
Rat LD_{50} dermal	> 2,000 mg/kg bw	
Rat LC_{50} inhalation	1.89 mg/L	R20
Skin irritation	non-irritant	
Eye irritation	Irritating to eyes	R36
Skin sensitization (test method used and result)	Magnusson & Kligman Test: sensitising	R43

Repeated dose toxicity

Species/ target / critical effect	Irritation of the gastro-intestinal tract, leading to hyperkeratosis of the oesophagus, hyperkeratosis and acanthosis in the non-glandular stomach in rats, reduced bodyweight gains and food intake in rats, mice and dogs. Vomiting in dogs, and poor general condition. Repeated dermal exposure resulted in irritation of the treated skin, but no systemic toxicity other than reduced body weight gains in males.
Lowest relevant oral NOAEL / LOAEL	10 mg/kg bw/day (dog, 12-month oral toxicity)
Lowest relevant dermal NOAEL / LOAEL	Males 10, Females >30 mg/kg bw/day (rat, 28-day dermal toxicity) LOAEL for local toxicity 1 mg/kg bw/d (rat, 28-day dermal toxicity)
Lowest relevant inhalation NOAEL / LOAEL	Not applicable.

Genotoxicity	Not mutagenic in vivo, but mutagenic in some in vitro tests. Considered non mutagenic as plant protection product active substance in EU review under Directive 91/414/EEC

Carcinogenicity

Species/type of tumour	Not carcinogenic in the rat. Treatment in the rat was associated with hyperkeratosis of the non-glandular stomach and of the oesophagus In the mouse, incidence of duodenal carcinomas and adenomas was increased, and folpet is considered carcinogenic in the mouse. A clear threshold of 20 mg/kg bw/d was established.

	Cat 3 R40
lowest dose with tumours	1,000 ppm (143 mg/kg bw/day)

Reproductive toxicity

Species/ Reproduction target / critical effect	No effects on reproduction (including the highest concentration tested – 3,600 ppm circa 180 mg/kg bw/day). Parental and offspring bodyweight effects at 800 ppm (40 mg/kg bw/day)
Lowest relevant reproductive NOAEL / LOAEL	NOAEL 180 mg/kg bw/day
Species/Developmental target / critical effect	Not teratogenic in rat or rabbit.
Developmental toxicity	
Lowest relevant developmental NOAEL / LOAEL	Maternal rat NOAEL 60 mg/kg bw/day Maternal rabbit NOAEL: 10 mg/kg bw/day No adverse effects were seen in rat foetuses at maternal doses up to and including 360 mg/kg bw/day, or in rabbit foetuses maternal doses up to and including 10 mg/kg bw/day. Reduced foetal weight in rat at 550 mg/kg bw/day and above, and in rabbit at 40 mg/kg bw/day.

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	Not neurotoxic
Lowest relevant developmental NOAEL / LOAEL.	NOAEL 10,000 ppm (equivalent to 1,138 - 474 mg/kg/day M, 1,140 – 595 mg/kg/day F)

Other toxicological studies

Mode of action	Folpet is an irritant. In the mouse this irritation causes changes to the architecture of the gastro-intestinal tract that are associated with the eventual tumour development. In the rat, irritation is seen primarily in the upper gastro-intestinal tract (e.g. oesophagus and non-glandular stomach), but these changes are not associated with tumour enhancement. As tumours are produced via an irritation mechanism, the appropriate risk assessment involves a margin of exposure evaluation (i.e. a threshold phenomenon). Folpet has essentially the same action as the closely-related compound captan. Oral ingestion results in the molecules passing from the stomach, where they are more stable in the relatively low pH of the mouse stomach, to the duodenum, where rapid hydrolysis takes place under alkaline conditions. Folpet is less stable than captan at low pH values, but both are highly unstable at high pH values. Folpet yields phthalimide, thiophosgene and two metabolites of phthalimide. Thiophosgene and the intact molecules react with the intestinal contents, and also encounter the mucous membrane of the villi. The action of folpet is local and is restricted to the villi cells. The villi cells have a short replacement time, as they are easily sloughed off. Replacement is by division of the crypt cells, and migration of the epithelial cells up the villi. The rapid degradation (hydrolysis) of both molecules restricts the effects to the initial contact. The

	molecules do not reach the crypt cells via the lumen, as the crypt cells are protected by their secretions. Degradation prevents effects occurring by way of diffusion through the villi cells to the crypt cells. Folpet reacts with soluble and insoluble thiols present in cells. Soluble thiols, such as glutathione, are available to react with and detoxify reactive molecules, whereas insoluble (or sensitive) thiols are necessary for normal cell function; reaction with these leads to disruption of cellular function. As the soluble thiol pool is depleted by high doses of folpet, the probability that sensitive thiols are disrupted increases. Both folpet and captan damage duodenal villi, and lead to increased proliferation of crypt cells as a homeostatic response to increase the rate of cell replacement. This mode of action is epigenetic. The mutagenicity studies show that while folpet can be mutagenic in vitro, it is not mutagenic in vivo. The activity in vitro is attenuated or eliminated in the presence of cysteine or other sources of thiols. In vivo, this attenuation is complete, and no activity is seen. The evidence demonstrates that while folpet is capable of inducing duodenal tumours in mice at high dose levels, the mechanism is not relevant at the low exposures anticipated for humans.
Further data on Folpet	Rat LD50 intraperitoneal: 52.5 mg/kg bw (males) and 48.0 mg/kg bw (females) at 24 hours

Medical data

	No indications of special concern in medical records or in relation to any reported medical incidents

Summary	Value	Study	Safety factor
Non-professional user			
ADI (acceptable daily intake, external long-term reference dose)	0.1 mg/kg bw/day	12-months oral chronic dog capsule study, 2-year rat study	100
AOEL-S (Operator Exposure)	0.2 mg/kg bw	Rabbit developmental toxicity	100
ARfD (acute reference dose)	0.2 mg/kg bw	Rabbit developmental toxicity	100
Professional user			
Reference value for inhalation (proposed OEL)	-	-	-
Reference value for dermal absorption concerning the active substance:	10%	EFSA agreed endpoint based on product studies	-
Reference value for dermal absorption concerning the representative product(s)[4]:	10%	EFSA agreed endpoint based on product studies	-

Chronic AEL (systemic) (mg/kg bw/day)	0.1 mg/kg bw/day	12-months oral chronic dog capsule study	100
Medium-term AEL	0.1 mg/kg /day	Rabbit developmental toxicity	100
Acute AEL	0.2 mg/kg bw	Rabbit developmental toxicity	100
Drinking water limit (mg/L)	300 µg/L	Derived from ADI	Not applicable

Acceptable exposure scenarios (including method of calculation)

Professional users	Acceptable for proposed uses according to model calculations
Production of active substance:	Acceptable for proposed uses according to model calculations
Formulation of biocidal product	Acceptable for proposed uses according to model calculations
Intended uses	Acceptable for proposed uses according to model calculations
Secondary exposure	Acceptable for proposed uses according to model calculations
Non-professional users	Acceptable for proposed uses according to model calculations
Indirect exposure as a result of use	The risk of acute or chronic exposure to folpet for all non-users is considered to be negligible.

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	Estimated degradation at 12°C pH4 = 17.1 hours (mean) pH5 = 8.7 hours pH7 = 2.7 hours (mean) pH9 = 0.1 hours. At pH 5 the predominant degradate is phthalimide but there is a shift towards phthalic acid which becomes the predominant degradate at pH 9. Phthalimide is readily hydrolysed. Estimated rates at 12°C are: pH4 = 3695 hours pH7 = 88 hours pH9 = 5.0 hours (mean). Hydrolysis is the primary route of degradation for folpet in the aquatic environment.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	The instability of folpet towards chemical hydrolysis, even at low pH, means that photolysis is not a significant degradation pathway in the aquatic environment.
Readily biodegradable (yes/no)	Yes
Biodegradation in seawater	No data, not applicable
Non-extractable residues	Sediment unextracted residues increased to *ca* 25% AR between day 7 and day 14 but were declining at the end of the study at 100 days. Unextracted residues were shown to be mainly associated with the humin fraction, probably due to phthalate formation. The decline of unextracted residues is most probably due to anaerobic degradation of the bound phthalates resulting in methane production (not collected in the study resulting in low mass balance).
Distribution in water / sediment systems (active substance)	Folpet was rapidly degraded in both the overlying water and the whole system, with DT_{50} values of 0.014 to 0.018 days (equating to a worst-case value of 0.4 hours). The equivalent range of degradation rates at the EU average temperature of 12°C can be estimated to be 0.03 to 0.04 days.
Distribution in water / sediment systems (metabolites)	The major metabolites (>10% AR) recovered from the water phase were phthalimide (max. 20.4 to 26.0% AR at 4 h), phthalamic acid (max. 13.3% AR at 1h), phthalic acid (max. 26.3 to 37.5% AR at 1d), benzamide (max. 10.2% AR at 1 d) and 2-cyanobenzoic acid (max. 39.7% AR at 1d). These metabolites were all readily degraded in the surface water phase and the whole system.

Route and rate of degradation in soil

Mineralization (aerobic)	Up to 60% after 90 days

Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20°C, aerobic): Folpet = 4.68 days (mean value concluded in the EFSA scientific report)[7]. Phthalimide = 7.88 days (mean value concluded in the EFSA scientific report). Phthalic acid = 1.37 days (mean value concluded in the EFSA scientific report). The geometric mean DT_{50} (12°C) for Folpet was determined to be 2.47 days. This is considered to be the correct DT_{50} value, however, as the EFSA agreed endpoint represents a worst-case value it has been used for risk assessment purposes.
	DT_{90lab} (20°C, aerobic): Folpet = 0.7 to 12.8 days (n = 3) Phthalimide = 1.7 to 16,1 days (n = 3) Phthalic acid = 2.1 to 13.7 days (n = 3)
	DT_{50lab} (10°C, aerobic): Folpet = 12.6 days Phthalimide = 10.6 days Phthalic acid = 5.9 days
	DT_{50lab} (25°C, anaerobic): Folpet = 13.8 to 14.6 days (n = 2) Phthalimide = 33.6 days
	degradation in the saturated zone: not relevant
Field studies (state location, range or median with number of measurements)	Field soil dissipation data show that degradation of folpet and phthalimide is rapid with the DT_{50} estimated to be less than 3 days for each substance. Highest residues were detected in the 0-15 cm soil horizon, with little or no movement to lower soil horizons. The field dissipation data confirms the results obtained from laboratory tests and shows that folpet and phthalimide (the principle soil metabolite) do not accumulate in soil.
Anaerobic degradation	Anaerobic degradation of folpet is slower under anaerobic conditions compared to aerobic conditions, resulting principally in the formation of phthalimide. However, folpet degradation under aerobic conditions is so rapid that behaviour under anaerobic conditions is not likely to be relevant.
Soil photolysis	Photodegradation is not a significant route of degradation for folpet.
Non-extractable residues	Levels of bound residues initially accumulated to a level of 31.2% AR at day 14, but subsequently declined resulting in substantial mineralisation to CO_2.
Relevant metabolites - name and/or code, % of applied active ingredient (range and maximum)	Phthalimide (max 65% AR after 5 days) Phthalamic acid (max 16.7% AR after 1 day) Phthalic acid (max 16.6% AR after 1 day) are the major (>10% AR) degradation products of folpet in soil. These compounds are also rapidly degraded in soil with DT_{50} values in the range of 0.5 to 4.8 days, 0.4 days and 0.6 to 4.1 days, respectively at 20°C. The equivalent range of

[7] The correct DT_{50} value is the geometric mean = 1.3 days at 20°C. The equivalent DT_{50} at 12°C = 2.47 days using TGD equation 25. The EFSA agreed endpoint represents a worst-case value and has been used in the risk assessment.

	soil degradation rates at the EU average temperature of 12°C can be estimated to be 1 to 10 days, 0.9 days and 1.3 to 8.7 days, respectively. Overall, phthalimide, phthalamic acid and phthalic acid are not considered to be persistent in soil.
Soil accumulation and plateau concentration	Folpet is not considered to be persistent in soil.

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	Adsorption/desorption coefficient of folpet cannot be reliably estimated by methods, such as the batch equilibrium method, because of rapid degradation in soil and in aqueous media. The lowest estimated adsorption/desorption coefficient is 304 mL/g. Adsorption/desorption coefficient of phthalimide was estimated in five soils of European origin using the batch equilibrium method. The Koc values determined for phthalimide were in the range 55.7 to 293.1 mL/g. Koc values for phthalamic acid and phthalic acid were determined by QSAR estimates in the range from 1.206 to 80.85 L/kg.

Fate and behaviour in air

Direct photolysis in air	Folpet degrades rapidly in air due to reaction with hydroxyl radicals with a half-life between 6.16 hours (QSAR estimation) and 1.02 days (EPA AOP v1.92 model based on 0.5 x 106 OH/cm3 and a 24 hour day).
Quantum yield of direct photolysis	No data, not relevant
Photo-oxidative degradation in air	No data, not relevant
Volatilization	The Henry's Law constant for folpet is 8 x 10^{-3} $Pa.m^3.mol^{-1}$. Folpet is a solid with a relatively high melting point and low vapour pressure and can therefore be considered as non-volatile. Concentrations in air are expected to be negligible during use and disposal

Monitoring data, if available

Soil (indicate location and type of study)	No data
Surface water (indicate location and type of study)	No data
Ground water (indicate location and type of study)	No data
Air (indicate location and type of study)	No data

Chapter 5: Effects on Non-target Species

Folpet: Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity (µg a.s./L)
Fish			
Oncorhynchus mykiss	96 hours (f-t)[a]	LC_{50}	15 (m m.)
Oncorhynchus mykiss	96 hours (s)[b]	LC_{50}	233 (nom)
Pimephales promelas	28 days, ELS (f-t)[a]	NOEC	8.1 (m m.)
Oncorhynchus mykiss	28 days (s-s)c, 3 renewals/week	LC_{50} NOEC	110 (nom.) 19 (nom)
Invertebrates			
Daphnia magna	48 hours (f-t)[a]	EC_{50}	20 (m m.)
Daphnia magna	48 hours (s)[b]	EC_{50}	> 1460 (m.m.i.)
Daphnia magna	21 days (f-t)[a]	NOEC	1.8 (m m.)
Daphnia magna	21 days (s-s)[c], 7 d renewal	NOEC	55 (m.m.i.)
Algae			
Desmodesmus subspicatus	72 hours (s)[b]	E_rC_{50} NOEC	> 10000 (nom.) 700 (nom.)
Microorganisms			
Activated sludge respiration (N & C oxidation combined)	3 hours (s)	EC_{50} NOEC	> 320000 (nom.) 10000 (nom.)
Activated sludge nitrification (NO_3 formation)	4 hours (s)	EC_{50} NOEC	> 1000000 (nom.) 32000 (nom.)

s: static exposure;
s-s: semi-static exposure;
f-t: flow-through exposure;
m m. based on mean measured concentrations covering entire test duration;
m m.i. based on mean measured initial concentration(s);
nom. based on nominal concentrations;
[a] continuous media renewal to counteract hydrolysis and maintain exposure to folpet a.s.;
[b] folpet allowed to hydrolyse, exposure mainly to hydrolysis degradates following brief initial exposure to a.s.
[c] folpet allowed to hydrolyse, exposure mainly to hydrolysis degradates, with brief exposure to a.s. at test initiation and following each media renewal.

Folpet metabolite Phthalimide: Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity (µg/L)
Fish			
Lepomis macrochirus	96 hours (s-s, 48 h renewal)	LC_{50}	38000 (m.m.)
Invertebrates			
Americamysis bahia	96 hours (f-t)	LC_{50}	12100 (m.m.)

s-s: semi-static exposure;
f-t: flow-through exposure;
m m. based on mean measured concentrations covering entire test duration.

Folpet metabolite Phthalic acid: Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity (µg/L)
Fish			
Oncorhynchus mykiss	96 hours (s)	LC_{50}	> 100000 (nom.)
Invertebrates			
Daphnia magna	48 hours (s)	EC_{50}	> 100000 (nom.)
Algae			
Pseudokirchneriella subcapitata	72 hours (s)	E_rC_{50} NOEC	> 10000 (nom.) 25000 (nom.)
s: static exposure; nom. based on nominal concentrations.			

Folpet metabolite Phthalamic acid: Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity (µg/L)
Fish			
Oncorhynchus mykiss	96 hours (s)	LC_{50}	> 100000 (nom.)
Invertebrates			
Daphnia magna	48 hours (s)	EC_{50}	> 100000 (nom.)
Algae			
Pseudokirchneriella subcapitata	72 hours (s)	E_rC_{50} NOEC	> 100000 (nom.) 100000 (nom.)
s: static exposure; nom. based on nominal concentrations.			

Folpet metabolite Benzamide: Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity (µg/L)
Fish			
Oncorhynchus mykiss	96 hours (s)	LC_{50}	> 100000 (m m.)
Invertebrates			
Daphnia magna	48 hours (s)	EC_{50}	> 102000 (m m.)
Algae			
Pseudokirchneriella subcapitata	72 hours (s)	E_rC_{50} NOEC	> 96000 (m.m.) 96000 (m.m.)
s: static exposure; nom. based on nominal concentrations.			

Folpet metabolite 2-Cyanobenzoic acid: Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity (µg/L)
Fish			
Oncorhynchus mykiss	96 hours (s)	LC_{50}	> 100000 (nom.)
Invertebrates			
Daphnia magna	48 hours (s)	EC_{50}	> 100000 (nom.)

Folpet metabolite 2-Cyanobenzoic acid: Toxicity data for aquatic species (most sensitive species of each group)

Algae			
Pseudokirchneriella subcapitata	72 hours (s)	E_rC_{50} NOEC	> 100000 (nom.) 100000 (nom.)
s: static exposure; nom. based on nominal concentrations.			

Effects on earthworms or other soil non-target organisms

Acute toxicity to *Eisenia foetida*	14-day LC_{50} > 1000 mg **folpet**-equiv/kg dry weight artificial soil, corresponding to > 882 mg folpet-equiv/kg on a wet weight basis.
Reproductive toxicity to *Eisenia foetida*	28-day NOEC = 5.18 mg **folpet**-equiv/kg dry weight artificial soil, corresponding to 4.57 mg folpet-equiv/kg on a wet weight basis. *
	28-day NOEC = 56.7 mg **phthalimide**/kg dry weight artificial soil (highest concentration tested), corresponding to 50.0 mg phthalimide/kg on a wet weight basis.
	28-day NOEC = 56.7 mg **phthalic acid**/kg dry weight artificial soil (highest concentration tested), corresponding to 50.0 mg phthalic acid/kg on a wet weight basis.
Terrestrial plant toxicity	The effects of soil (LUFA 2.2)-incorporated **phthalimide** on seedling emergence and early growth stage seedling development were studied according to OECD 208. The most sensitive species was sugar beet (*B. vulgaris*): the lowest EC_{50} was 193 mg phthalimide/kg soil dw. The corresponding NOEC was 64 mg/kg soil dw and the lowest EC_{10} was 58.5 mg/kg soil dw (51.6 mg/kg wet weight).
	The effects of soil (LUFA 2.2)-incorporated **phthalic acid** on seedling emergence and early growth stage seedling development were studied according to OECD 208. The most sensitive species was carrot (*D. carota*): the NOEC was 64 mg/kg soil dw and the lowest EC_{10} was 44.3 mg/kg soil dw (39.1 mg/kg wet weight).
* Agreed by EPCO 22 experts meeting on ecotoxicology that the lowest endpoint should be used without applying a correction factor. Folpet added at test initiation is expected to have been hydrolysed under the conditions of these studies and the influence of the metabolites is therefore accommodated within the endpoints.	

Effects on soil micro-organisms

Nitrogen mineralization	No significant effects of folpet (<±10% effect compared to untreated control) at 1.874 and 18.74 mg a.s./kg wet soil (1.593 and 15.93 kg folpet/ha).
Carbon mineralization	Dehydrogenase activity affected by < 10% (compared to untreated control) at 1.874 mg **folpet**/kg wet soil (1.593 kg folpet/ha). Effect >10%, <25% on D 28 at 15.93 kg a.s./ha (15.93 kg a.s./ha). NOEC therefore set to 1.874 mg folpet/kg wet soil).
	NOEC based on statistically significant ($p < 0.05$) inhibition of glucose-induced respiration (C-mineralisation) in LUFA 2.3 soil was 1000 mg **phthalimide**/kg dry soil, corresponding to 882 mg phthalimide/kg wet soil.
	NOEC based on statistically significant ($p < 0.05$) inhibition of glucose-induced respiration (C-mineralisation) in LUFA 2.3 soil was 400 mg **phthalic acid**/kg dry soil, corresponding to 353 mg phthalic acid/kg wet soil.

Effects on terrestrial vertebrates

Acute toxicity to mammals	LC_{50} > 2000 mg/kg bw (rat).
Acute toxicity to birds	LD_{50} = 2510 mg/kg bw (bobwhite quail).
Dietary toxicity to birds	LC_{50} >5000 ppm (bobwhite quail, mallard duck).
Reproductive toxicity to birds	NOEC = 1000 mg/kg diet (bobwhite quail, mallard duck).

Effects on honeybees

Acute oral toxicity	LD_{50} > 236 µg/bee.
Acute contact toxicity	LD_{50} > 200 µg/bee.

Bioconcentration

Bioconcentration factor (BCF)	Whole fish BCF = 56.
Depuration time(DT_{50}) (DT_{90})	0.63.
Level of metabolites (%) in organisms accounting for > 10 % of residues	Levels < 10% following 14-day depuration phase.

Chapter 6: Other End Points

Not applicable.

Appendix II: List of Intended Uses

Folpet is used as a film preservative (PT 7) for use in products including paints, mastics, sealants, fillers and adhesives showing a preservative effect (e.g. wallpaper paste). Products containing folpet may be used by professionals (decorators and builders) and non-professionals. Typical application is manual (by brush, roller or spray apparatus).

The function is fungicide and the maximum end use concentration of folpet in the treated paint is 2g a.s./kg.

Organisms to be controlled are fungal species (*Candida albicans).*

The active substance, folpet, is applied once to the treated article during manufacture. The active substance, folpet, is not used directly by users.

Use assumptions based on the available guidance are as follows:

- Professional user: brush and roller application, 360 mins per day. Daily use.
- Professional user: spray application, 360 minutes per day.
- Non-professional user: brush and roller application, 4 hours per day, 2 to 5 days per year.

The biocidal product for PT 7 film preservative use is folpet technical. Adequate existing data were provided and accepted in support of these intended uses.

Object and/or situation	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment			Remarks:
			Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	number min max	interval between applications (min)	g a.s./L min max	water L/m^2 min max	g a.s./m^2 min max	
Paints, mastics, sealants, fillers and adhesives showing a preservative effect (e.g. wallpaper paste)	Folpet	*Candida albicans*	Powder or crystals	Max. 2g a.s./kg	Applied once to the treated article during manufacture	1	Not applicable	Not applicable	Not applicable	Not applicable	None

Appendix III: List of studies

Data protection is claimed by the applicant in accordance with Article 60 of Regulation (EU) No 528/2012.

IIIA reports

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No	Owner
Section 2					
IIIA 2.7/01	Schlesinger, H.M.	1996	Folpet (folpan) technical. Analysis and certification of product ingredients. Analyst Ltd., Report No. 47/95 (Company file: R-8122). GLP, Unpublished. CONFIDENTIAL	Y	Makhteshim
IIIA 2.7/02	Anon	2006	Folpet. a. i. technical specification. Makhteshim Chemical Works Ltd., unnumbered report, 31 January 2006. Not GLP, Unpublished. CONFIDENTIAL	Y	Makhteshim
Section 3					
IIIA 3.1.1/01	Volante, A.	1995a	Determination of the melting point of folpan. Institut Fresenius, Report No. IF-94/09656-01 (Company file: R-7883). GLP, Unpublished.	Y	Makhteshim
IIIA 3.1.3/01	Volante, A.	1995b	Determination of the density of folpan. Institut Fresenius, Report No. IF-94/09656-02 (Company file: R-7884). GLP, Unpublished.	Y	Makhteshim
IIIA 3.2/01	Lorence, P.J.	1991	Folpet – determination of vapor pressure. Ricerca Inc., Report No. 4174-91-0098-AS (Company file: R-6280). GLP, Unpublished.	Y	Makhteshim
IIIA 3.3.1/01	Schlesinger, H.M.	1987a	Folpan – water solubility. Analyst Ltd., Report No. 431 (Company file: R-4626). Not GLP, Unpublished.	Y	Makhteshim
IIIA 3.3.1/02	Schlesinger, H.M.	1987b	Folpan – solubility in organic solvents. Analyst Ltd., Report No. 436 (Company file: R-4636). Not GLP, Unpublished.	Y	Makhteshim
IIIA 3.3.1/03	Schlesinger, H.M.	1987c	Folpan – partition coefficient (n-octanol/water). Analyst Ltd., Report No. 426 (Company file: R-4616). Not GLP, Unpublished.	Y	Makhteshim
IIIA 3.3.1/04	Comb, A.L.	1998	Folpet (technical) physico-chemical properties. Huntingdon Life Sciences Ltd., Report No. MAK502/983411 (Company file: R-10248).	Y	Makhteshim

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No	Owner
			GLP, Unpublished.		
IIIA 3.3.2/01	Schlesinger, H.M.	1987a	Folpan – water solubility. Analyst Ltd., Report No. 431 (Company file: R-4626). Not GLP, Unpublished.	Y	Makhteshim
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IIIA 4.2(a)/01	Rose, J.E., Kimmel, E.	2000	Field soil dissipation of folpet in bare soil in Washington. PTRL West, Inc., Report No. 915W-1 (Company file: R-11798). GLP, Unpublished.	Y	Makhteshim
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IIIA 6.2/06	van de Sandt, J.J.M.	1997	*In vitro* percutaneous absorption of formulated Folpan^{TM} (folpet) through human and rat skin. TNO Nutrition and Food Research Institute, Report No. V97.550. (Company file: R-9424a). GLP, Unpublished.	Y	Makhteshim
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IIIA 7.1.1.2.1/01	Jenkins, W.R.	1994	Folpet technical: assessment of its ready biodegradability. Pharmaco-LSR Ltd., Report No. 94/MAK/186/0048 (Company file: R-7491). GLP, Unpublished.	Y	Makhteshim
IIIA 7.1.1.2.1/02	Jenkins, W.R.	1998	C^{14}-Folpet: assessment of its ready biodegradability. HLS Ltd., Report No. MAK512/984038 (Company file: R-10488). GLP, Unpublished.	Y	Makhteshim
IIIA 7.1.2.2.2/01	Crowe, A.	1999	Folpet. Degradability in the water/sediment system. HLS Ltd., Report No. MAK 510/98502 (Company file: R-10432). GLP, Unpublished	Y	Makhteshim
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IIIA 7.2.2.2/03	Rose, J.E., Kimmel, M.	2000	Field soil dissipation of folpet in bare ground in Washington. PTRL West, Inc. Report No. PTRL 915W-1 (Company file R-11798). GLP, Unpublished..	Y	Makhteshim
IIIA 7.2.2.4/01	Daly, D.	1991b	Anaerobic soil metabolism of ^{14}C-folpet. ABC Laboratories, Inc., Report No. 37156. (Company file: R-5473). GLP, Unpublished.	Y	Makhteshim
IIIA 7.2.2.4/02	Pack, D.E.	1980	The anaerobic soil metabolism of (carbonyl-^{14}C) Folpet. Chevron Chemical Company, Report No. 721.14 (Company file: R-7031). Not GLP, Unpublished.	Y	Makhteshim
IIIA 7.2.2.4/03	Rhoads, W.D.	1991a	Environmental fate study for soil photolysis characteristics of folpet under natural and artificial light. Colorado Analytical Research & Development Corporation, Report No. Makhteshim 1096 (Company file: R-5270). GLP, Unpublished.	Y	Makhteshim
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