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

Evaluation of active substances

COMPETENT AUTHORITY REPORT

Fludioxonil

Product type 7, 9 and 10

(Film preservatives; Fibre, rubber and polymerised materials preservatives, Construction material preservatives)

Evaluating Competent Authority: Denmark

April 2017

Substance Name: Fludioxonil

EC Name: 4-(2,2-difluoro-1,3-benzodioxol-4-y1)-1H-pyrrole-3-carbonitrile

EC Number: Not allocated

CAS Number: 131341-86-1

Applicant: LANXESS Deutschland GmbH

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1. STATEMENT OF SUBJECT MATTER AND PURPOSE

This assessment report has been established as a result of the evaluation of a new active substance Fludioxonil in product-type 7, 9 and 10 (film preservatives; fibre, leather, rubber and polymerised materials preservatives; construction material preservatives), carried out in the context of Regulation (EU) No 528/2012, with a view to the possible approval of this substance.

On October 8, 2014 the Danish competent authorities received a dossier (payment) from the applicant. The Evaluating Competent Authority accepted the dossier as complete for the purpose of the evaluation on January 13, 2015.

On April 5, 2016 the Evaluating Competent Authority submitted to ECHA a copy of the assessment report containing the conclusions of the evaluation, hereafter referred to as the competent authority report (CAR). Before submitting the CAR to ECHA, the applicant was given the opportunity to provide written comments in line with Article 8(1) of Regulation (EU) No 528/2012.

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

The aim of the assessment report is to support the opinion of the Biocidal Products Committee and a decision on the approval of Fludioxonil for product-type 7, 9 and 10 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 the assessment report, which is available from the web-site of ECHA shall be taken into account.

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. CONCLUSION

The outcome of the assessment of fludioxonil product-types 7, 9 and 10 is specified in the BPC opinions following discussions at the 19. meeting of the Biocidal Products Committee (BPC). The BPC opinions are available from hte ECHA web-site.

Requirement for further information related to the reference biocidal product

Not relevant.

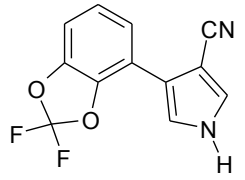
3. ASSESSMENT REPORT

Study summaries and background documents for fludioxonil and the representative product can be found in IUCLID for PT7, 9 and 10.

Summary

1 PRESENTATION OF THE ACTIVE SUBSTANCE

1.1 IDENTITY OF THE ACTIVE SUBSTANCE

Main constituent(s)	
ISO name	Fludioxonil
IUPAC or EC name	4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1H-pyrrole-3-carbonitrile
EC number	no entry
CAS number	131341-86-1
Index number in Annex VI of CLP	608-RST-VW-Y
Minimum purity / content	95 %
Structural formula	

Relevant impurities and additives		
IUPAC name or chemical name or EC name	**Maximum concentration in % (w/w)**	**Index number in Annex VI of CLP**
sodium 4-toluene sulphonate (SYN549410)	5 g/kg	**-**
1-[2-cyano-1-(2,2-difluoro-1,3-benzodioxol-4-yl)ethyl]-4-(2,2-difluoro-1,3-benzodioxol-4-yl)pyrrole-3-carbonitrile (SYN549129)	1 g/kg	**-**

1.2 INTENDED USES AND EFFECTIVENESS

Use of the active substance:

Product type	Fungicide for material preservation in PT7, PT9 and PT10.
Intended use pattern(s)	PT7 Film preservatives For PT7 uses, fludioxonil is formulated as the preservative product "Sporgard WB" which is added to paints, silicon coatings, mineral sealants and grouts. Other preservative products containing fludioxonil may be used in silicon sealants and grout. End-products will only be used indoor. PT9 Fibre, leather, rubber and polymerised material preservatives For PT9 uses, fludioxonil is formulated as the preservative product "Sporgard WB" which is added to paper that is used for the production of wall linings. End-products will only be used indoor. PT10 Masonry preservatives For PT10 uses, fludioxonil is formulated as the preservative product "Sporgard WB" which is added to building materials such as gypsum boards. End-products will only be used indoor.
Users	Fludioxonil in combination with other fungicides are added during material production. The end-use treated items may be used by professional workers and by the general public (non-professional), depending on the individual item.

Effectiveness of the active substance:

Function	Fludioxonil is used in biocidal preservative products which are applied to, or incorporated into various end-applications covering protection of paper, wall boards, masonry and coating/sealing products. Fludioxonil is not intended to be used as a stand-alone substance; it is intended to be used in combination with other fungicides.
Organisms to be controlled	Biocidal products containing *inter alia* the active substance fludioxonil are intended to inhibit the growth of fungi associated with odours, staining and, in general, bio-deterioration. Target fungi includes in example *Alternaria alternata* and *Stachybotrys chartarum*. Fludioxonil provides innate activities against some *Penicillium* spp., *Alternaria* spp., *Stachybotrys chartarum* and some wood decaying fungi, such as *Conophora puteana*, *Gloeophyllum trabeum* and *Sydowia pythiophila*. Whereas no activity was found against in example *Aureaobasidium pululans*,

	Chaetomium globosum and *Trichoderma viride*.
Limitation of efficacy including resistance	Fludioxonil has a single site mode of action and is therefore more prone to the development of resistance, because any change(s) that might occur in the fungus to alter that single site could render the fungus resistant to the fungicide. The potential for resistance development therefore exists, but is restricted, because fludioxonil will be used in combination with other fungicides, that present different modes of action and thereby ensuring that resistance potential is limited.
Mode of action	Fludioxonil is a fungicide that works by inhibiting the osmotic signal pathway which results in the inhibition of spore germination and prevention of mycelia growth. The mode of action of fludioxonil is by inhibition of a mitogen-activated protein (MAP) kinase in signal transduction of osmo-regulation (glycerol synthesis). Fludioxonil acts immediately on the target mode of action and there is no time delay for efficacy.

1.3 CLASSIFICATION AND LABELLING

1.3.1 Classification and labelling for the active substance

Hazard class/ property	Proposed classification
Physical hazards	
No physical hazard	
Human health hazards	
No human health hazard	
Environmental hazards	
Aquatic acute 1	H400: Very toxic to aquatic life (M=1)
Aquatic chronic 1	H410: Very toxic to aquatic life with long lasting effects (M=1)

Current Classification and Labelling according to Regulation (EC) No 1272/2008:

There is no current classification according to Regulation (EC) No 1272/2008 for fludioxonil; however a classification proposal is sent to ECHA in 2015, find the proposed classification and labelling in the following table.

Classification		Labelling					
Hazard Class and Category	**Hazard statements**	**Pictograms**	**Signal word**	**Hazard statements**	**Suppl. Hazard statements**	**Precautionary statements**	**SCLs and M-factors**
Aquatic Acute 1 Aquatic Chronic 1	H400 H410		Warning	H410: Very toxic to aquatic life with long lasting effects		P273 P391 P501	M = 1 M = 1

Current Classification and Labelling according to the Directive 67/548/EEC:

Fludioxonil is not listed on Annex I of Directive 67/548/EEC. Fludioxonil is listed on Annex I of Directive 91/414/EEC; classification was conducted during the evaluation under Directive 91/414/EEC. This is the classification suggested during the evaluation under Directive 91/414/EEC.

Classification		Labelling			
Indications of danger	**R-phrases**	**Indications of danger**	**R-phrases**	**S-phrases**	**Concentration limits**
N	R50/53		R50/53		

1.3.2 Classification and labelling for the representative product(s)

Proposed Classification and Labelling according to Regulation (EC) No 1272/2008:

Classification		Labelling					
Hazard Class and Category	**Hazard statements**	**Pictograms**	**Signal word**	**Hazard statements**	**Suppl. Hazard statements**	**Precautionary statements**	**SCLs and M-factors**
Aquatic Acute 1 Aquatic Chronic 1	H400 H410		Warning	H410: Very toxic to aquatic life with long lasting effects.	EUH208: Contains BIT. May produce an allergic reaction.	P273 P391 P501	

Proposed Classification and Labelling according to the Directive 1999/45/EC:
Only a proposed classification according to Regulation (EC) No 1272/2008 is included.

Packaging of the biocidal product:

Type of packaging	Size/volume of the packaging	Material of the packaging	Type and material of closure(s)	Intended user (e.g. professional, non-professional)	Compatibility of the product with the proposed packaging

					materials (Yes/No)
IBC (Intermediate bulk container)	1100 kg	Plastic (HDPE)	Steel cage (not in contact with the product)	Professional user	Yes
Drum	200 kg	Plastic (HDPE)	Tight head HDPE drum with LDPE safety cap.	Professional user	Yes

2 SUMMARY OF THE HUMAN HEALTH RISK ASSESSMENT

Summary of the assessment of effects on human health

Endpoint	Brief description
Toxicokinetics	*More than 80% of Fludioxonil is absorbed after oral administration of a single oral dose.* *Fludioxonil is uniformly distributed (with the highest residues found in liver and kidneys) and does not show any potential for accumulation.* *Fludioxonil is excreted via urine (13-20 %) and faeces (about 68 %) within 24 hours from administration. The excretion was mainly via the bile.* *Fludioxonil is extensively metabolised (fludioxonil was detected in faeces but not in the urine). The major metabolic pathway is oxidation at position 2 of the pyrrole ring; two minor pathways are oxidation at position 5 of the pyrrole ring and hydroxylation of the phenyl ring.* *A default value of 100 % is used for inhalatory absorption (no study was performed).*
Acute toxicity	*Fludioxonil is not acutely toxic via oral, dermal and inhalation route (LD50>5000 mg/kg/bw, LD50 >2000 mg/kg bw and LC50 >2.6 mg/L air/4h (nose-only), respectively).*
Corrosion and irritation	*Fludioxonil is not skin and eye irritant.*
Sensitisation	*Fludioxonil is not a skin sensitiser.*
Repeated dose toxicity	*Target organs after repeated oral administration are the liver (increased weight & hepatocyte hypertrophy) in all three species rats, mice and dogs and bile duct proliferation and kidney effects (increased weight, nephropathy) in rats and mice and signs of mild anemia in the 90 days dog study (not observed in the 1 year dog).* *The relevant sub chronic oral NOAEL is 58.5 mg/kg bw/day from the 90-day study in dog. In the 1 year dog study a NOAEL of ~33 mg/kg/bw day were established based on similar effects (as in the 90 days study) at the highest dose levels at 298 mg/kg/bw day.* *The relevant chronic oral NOAEL is 37 mg/kg bw/day from the 2 year rat study.* *The NOAEL from the repeated dose dermal study in rats is 200 mg/kg bw/day based on the only treatment-related effects observed on thymus in high dose females. No such effects was observed in males. No other studies confirmed this finding.*
Genotoxicity	*Negative results are reported for gene mutation in vitro in an Ames test and a study of mammalian cell mutation. Fludioxonil showed a clastogenic potential in vitro, but in vivo no clastogenic potential were observed in the bone marrow of the Chinese hamster, in the bone marrow of the mouse and no indication of DNA repair as result of DNA damage were observed in the rat hepatocytes.* *On the basis of the available information it was concluded that overall*

	fludioxonil is not genotoxic or mutagenic. *Note: This is consistent with the EFSA conclusion from 2007 which is based on the same data.*
Carcinogenicity	*An increased incidence of hepatocellular tumours was present in rats. However, for male rats the incidences did not exhibit a dose-response relationship. For female rats the increased incidence in high-dose females was not statistically significantly different from that in the control group and within the historical control data of the laboratory.* *Therefore the hepatocellular tumours observed were not considered treatment-related.* *The incidences of lymphomas, metastatic multicentric neoplasms and total neoplasms were high in female mice at 3000 ppm but were within the historical control data of the laboratory. The incidences in the two higher doses of 5000 and 7000 ppm were both similar to the two controls groups. As there is no dose response it was concluded they were not related to the treatment.* *Overall, Fludioxonil was considered not to be carcinogenic to either rats or mice.*
Reproductive toxicity	*Fludioxonil did not show reproductive and developmental toxicity potential.* *Fludioxonil was not toxic to reproduction in the two-generation study in rats at daily dietary doses up to 212 mg/kg bw/day, a dose level at which parental toxicity was observed.* *In the developmental toxicity studies in rats and rabbits, no effects on the foetuses were observed at any dose level even though maternal toxicity (reduced bw gain) occurred at the high dose levels (1000 mg/kgbw/day in rats, 300 mg/kg bw/day in rabbits).*
Neurotoxicity	*Fludioxonil has no structural relationship to neurotoxic substances. Moreover no evidence of neurotoxic potential are seen in the toxicological studies.*
Immunotoxicity	*No evidence of immunotoxicity was seen in any of the standard toxicity studies performed with fludioxonil. The structure and mechanism of action of fludioxonil do not raise any concerns of relevance to immunotoxicity.*
Disruption of the endocrine system	*Some effects were reported in a published study (in vitro study with MCF-7 human breast cancer cell line in a non-validated test system).* *In the Tox21 programme (phase II) fludioxonil was clustered together with other oestrogenic compounds based on similar activity profiles.* *No signs of endocrine-related findings were observed in the standard in vivo mammalian toxicity studies. The exclusion criteria in BPR Article 5(1)a-c, d are not met. It is therefore not justified to conclude that the findings in the published study/Tox21 programme might give raise to specific concerns of relevance to endocrine disruption by fludioxonil in vivo.*
Other effects	*No data.*

Reference values

	Study	**NOAEL/ LOAEL (mg/kg bw /day)**	**Overall assessment factor**	**Value (mg/kg bw /day)**
$AEL_{acute/short-term}$	28 day oral rat study	100 (1000)	100	1
$AEL_{medium-term}$	90 day oral dog study	59 (299)	100	0.59
$AEL_{long-term}$	2 year oral rat study	37 (113)	100	0.37

Risk characterisation

Summary table: scenarios for PT7			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
PT7-1	Mix/load	**Primary:** Mixing and loading, i.e., blending of the biocidal product (b.p.) into the paint	Industrial (PT7)
PT7-2	Maintenac e of machines	**Primary:** Maintenance work is done for the different parts of production machines.	Industrial (PT7)
PT7-3	Spray application	**Primary:** Applying preserved water-based paints by spraying	Professional (PT7)
PT7-4	Brush and roller application	**Primary:** Applying preserved water-based paints using a brush or roller	Professional (PT7)
PT7-5	Application of mineral sealants and grout	**Primary:** Applying preserved mineral sealant or grout	Professional (PT7)
PT7-6	Wash out paint brush	**Primary:** Washing out paint brushes after application	Professional(PT7)
PT7-7	Spray equitment cleaning	**Primary:** Cleaning of spray equipment after application	Professional (PT7)
PT7-8	Spray application	**Primary:** Applying preserved water-based paints by spraying	Non-professional (PT7)
PT7-9	Brush and roller application	**Primary:** Applying preserved water-based paints using a brush or roller	Non-Professional (PT7)
PT7-10	Application of mineral sealants and grout	**Primary:** Applying preserved mineral sealant or grout	Non-Professional (PT7)
PT7-11	Wash out paint brush	**Primary:** Washing out paint brushes after application	Non-professional (PT7)
PT7-12	Spray equiptmen t cleaning	**Primary:** Cleaning of spray equipment after application	Non-professional (PT7)
PT7-13	Toddler	**Secondary (in direct exposure):** Toddler – touching wet painted surface	General public (PT7)
PT7-14	Toddler	**Secondary (in direct exposure):** Toddler – touching wet painted surface and mouthing	General public (PT7)

PT7-15	Toddler	**Secondary (indirect exposure)** Toddler – touching dried painted surface	General public (PT7)
PT7-16	Toddler	**Secondary (indirect exposure)** Toddler – touching dried painted surface and mouthing	General public (PT7)
PT7-17	Adult	**Secondary (indirect exposure)** Adult –laundry of contaminated coveralls after paint spraying activities	General public (PT7)
PT7-18	Toddler	**Secondary (in direct exposure):** Toddler – dermal contact with wet preserved materials (e.g. mineral sealants and grouts)	General public (PT7)
PT7-19	Toddler	**Secondary (in direct exposure):** Toddler – dermal contact with wet preserved materials (e.g. mineral sealants and grouts) and mouthing	General public (PT7)
Scenario (screening) Long term inhalation exposure for volatilised active substance	Toddler	**Secondary (indirect exposure):** Toddler – inhalation exposure to volatilized residues	General public (PT7)
PT7-20	Adult	**Secondary (indirect exposure)** Adult (professional worker) – removing dried preserved paint and sealant by sanding	Professional (PT7)
PT7-21	Adult	**Secondary (indirect exposure)** Adult (non-professional) – removing dried preserved paint and sealant by sanding	Non-professional (PT7)

Summary table: scenarios for PT9			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure** **Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
PT9-1	Mix/load	**Primary:** Mixing and loading; handling concentrate for PT 9.02 uses – paper for drywall manufacture	Industrial (PT9)

Summary table: scenarios for PT10			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
PT10-1	Mix/load	**Primary:** Mixing and loading; handling concentrate during gypsum powder/dry wall manufacture	Industrial (PT10)
PT10-2	Cutting /sawing	**Primary:** Professional cutting/sawing or drilling gypsum drywall	Professional (PT10)
PT10-3	Cutting /sawing	**Primary:** Non-professionel cutting/sawing or drilling gypsum drywall	Non-professional (PT10)

Conclusion of risk characterisation for industrial user

Scenario, Tier, PPE		**Relevant reference value** (mg/kg bw/d)	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
Mixing and loading phase: Industrial worker handling concentrate for PT7 (paint), PT9.02 (paper for drywall manufacture) & PT10 (gypsum powder/drywall manufacture) RISKOFDERM – Loading liquid, automated or semi-automated (HEEG, 2008). Task duration 10 min **Maintenace of machines (PT7-2)** Industrial worker conducting maintenance work done for the different parts of the production machines (used in paint manufacture and formulation) ECHA Biocides Guidance 2015: Biocides Human Health Exposure Methodology (dermal algorithm)					
PT7-1	I	$AEL_{long\ term}$ = 0.37	1.0×10^{-2}	2.8	yes
	II (gloves, coverall)		1.1×10^{-3}	0.3	yes
PT7-2	I	$AEL_{long\ term}$ = 0.37	0.46	123.2	No
	II (gloves)		4.6×10^{-2}	12.3	Yes
PT9-1	I	$AEL_{long\ term}$ = 0.37	1.0×10^{-2}	2.8	yes
	II (gloves, coverall)		1.1×10^{-3}	0.3	yes
PT10-1	I	$AEL_{long\ term}$ = 0.37	1.0×10^{-2}	2.8	yes
	II (gloves, coverall)		1.1×10^{-3}	0.3	yes

Systemic exposures to fludioxonil in industrial workers associated with mixing and loading the Sporgard WB biocidal product (containing up to 2% w/w fludioxonil) during the PT7 uses as paint manufacturing/formulating processes, PT9 uses as drywall paper manufacturing processes and PT10 uses as drywall gypsum manufacturing processes (e.g. connecting and disconnecting the concentrated product

to the dosage pump via transfer lines) were determined using the default data in the HEEG *Opinion on the use of available data and models for the assessment of the exposure of operators during the loading of products into vessels or systems in industrial scale* (April 6, 2008) for liquid (semi-) automated transfer/pumping processes (the approach used is discussed in detail under section "8. Human exposure assessment"). A tiered approach was used, taking into account PPE, as appropriate.
The results of the risk assessment for systemic effects, takes into account a dermal absorption values of 3%.

"Based on the predicted exposures and risk characterisation for systemic effects, the handling of Sporgard WB concentrate during the manufacture of end-use products by industrial workers is not considered to pose an unacceptable risk to human health with PPE."

Conclusion of risk characterisation for professional user (primary exposure scenarios)

Scenario, Tier, PPE		Relevant reference value (mg/kg bw/d)	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
Preserved film products (PT7)					
PT7-3 Spray application	I (gloves)	$AEL_{long\ term}$ = 0.37	2.7×10^{-2}	7.4	Yes
	IIa (gloves, coverall)		1.0×10^{-2}	2.8	Yes
	IIb (gloves, coverall& RPE)		5.5×10^{-3}	1.5	Yes
PT7-4 Brush and roller application	I	$AEL_{long\ term}$ = 0.37	1.0×10^{-2}	2.8	Yes
	II (gloves, coverall)		3.8×10^{-3}	1.0	Yes
PT7-5 Mineral sealants and grout application	I	$AEL_{long\ term}$ = 0.37	4.8×10^{-4}	0.13	Yes
	II (gloves)		4.8×10^{-5}	0.01	Yes
PT7-6 Wash out brush	I	$AEL_{long\ term}$ = 0.37	2.8×10^{-5}	7.5×10^{-3}	Yes
	II (gloves, coverall)		2.8×10^{-6}	7.5×10^{-4}	Yes
PT7-7 Cleaning of spray equitment	I	$AEL_{long\ term}$ = 0.37	3.7×10^{-4}	0.1	Yes
	II (gloves, coverall)		5.0×10^{-5}	0.01	Yes
Preserved masonry materials (PT10)					
PT10-2 Cuttting/ sawing	I	$AEL_{long\ term}$ = 0.37	8.0×10^{-5}	0.02	Yes
	II (gloves)		5.1×10^{-5}	0.01	Yes

Preserved film products (PT7)

Systemic exposures to fludioxonil in professional workers associated with mixing and loading, and applying end-use products preserved using Sporgard WB (containing up to 2% w/w fludioxonil) and cleaning equipment after use were determined using default scenarios in the EU TNsG, the HEEG opinion, ECETOC TRA model or the BEAT model (the approaches used are discussed in detail in the corresponding Document IIB). Separate calculations for the mixing and loading phase have not been

carried out since potential exposures are already accounted for in default data for the application phase. A tiered approach was used, taking into account PPE, as appropriate.

The results of the risk assessment for systemic effects, takes into account a dermal absorption values of 3%.
Based on the predicted exposures and risk characterisation for systemic effects, tasks involving the uses of end-use film products preserved using Sporgard WB carried out by professional workers are not considered to pose an unacceptable risk to human health neither with and without PPE.

Preserved materials (PT9)
There are no direct professional uses of drywall coating paper which has been treated with Sporgard WB as a preservative.

Preserved masonry materials (PT10)
Based on the predicted exposures and risk characterisation for systemic effects, tasks involving the use of preserved masonry products carried out by professional workers are not considered to pose an unacceptable risk to human health.

Conclusion of risk characterisation for non-professional user (primary exposure scenarios)

Scenario, Tier, PPE		Relevant reference value (mg/kg bw/d)	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
Preserved film products (PT7)					
PT7-8 Spray application	**Tier 1** (no PPE)	$AEL_{short-term}$ = 1	2.4×10^{-3}	0.24	Yes
PT7-9 Brush and roller application	**Tier 1** (no PPE)	$AEL_{short-term}$ = 1	5.8×10^{-4}	5.8×10^{-2}0.6	Yes
PT7-10 Mineral sealants and grout application	**Tier 1** (no PPE)	$AEL_{short-term}$ = 1	2.4×10^{-4}	1.3×10^{-2}	Yes
PT7-11 Wash out brush	**Tier 1** (no PPE)	$AEL_{short-term}$ = 1	2.8×10^{-5}	4.7×10^{-3}	Yes
PT7-12 Cleaning of spray equitment	**Tier 1** (no PPE)	$AEL_{short-term}$ = 1	3.7×10^{-4}	3.7×10^{-2}	Yes Yes
Preserved masonry materials (PT10)					
PT10-3 Cutting/sawing	**Tier 1** (no PPE)	$AEL_{short-term}$ = 0.59	3.6×10^{-5}	0.01	Yes

Preserved film products (PT7)

Based on the predicted exposures and risk characterisation for systemic effects, tasks involving the uses of end-use film products preserved using Sporgard WB carried out by non-professionals are not considered to pose an unacceptable risk to human health.

Preserved materials (PT9)
There are no direct professional uses of drywall coating paper which has been treated with Sporgard WB as a preservative.

Preserved masonry materials (PT10)
Based on the predicted exposures and risk characterisation for systemic effects, tasks involving the uses of preserved masonry products carried out by consumers are not considered to pose an unacceptable risk to human health.

Conclusion of risk characterisation for non-professionals (secondary (indirect) exposure scenarios)

Scenario, Tier, PPE		Relevant reference value (mg/kg bw/d)	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
Preserved film products (PT7)					
PT7-21 Sanding preserved paint and sealant	I (no gloves)	$AEL_{short-term} = 1$	1.0×10^{-2}	1.023	Yes

Preserved materials (PT7)

Based on the predicted exposures and risk characterisation for systemic effects, tasks involving the sanding of preserved dried paints or sealants carried out by non-professionals (i.e consumers), where secondary (indirect) exposures to fludioxonil may occur, are not considered to pose an unacceptable risk to human health.

Conclusion of risk characterisation for indirect exposure (general public)

Scenario, Tier	Relevant reference value (mg/kg bw/d)	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
Scenario [PT7-13] Toddler-touching wet painted surface	$AEL_{short\text{-}term}$ = 1	1.3 x 10^{-3}	0.13	Yes
Scenario [PT7-14] Toddler-touching wet painted surface and mouthing	$AEL_{acute}/_{short\text{-}term}$ = 1	5.6 x 10^{-3}	0.56	Yes
Scenario [PT7-15] Toddler touching dried painted surface	$AEL_{acute}/_{short\text{-}term}$ = 1	5.6x10^{-5}	5.6 x 10-3	Yes
Scenario [PT7-16] Toddler touching dried painted surface and mouthing	$AEL_{acute}/_{short\text{-}term}$ = 1	1.0x10^{-3}	0.1	Yes
Scenario [PT7-17] Adult-laundry of contaminated coveralls	$AEL_{medium\text{-}term}$ = 0.59	7.6 x 10^{-4}	0.13	Yes
Scenario [PT7-18] Toddler-dermal contact with wet preserved materials	$AEL_{acute}/_{short\text{-}term}$ = 1	2.2 x 10^{-4}	2.2 x 10^{-2}	Yes
Scenario [PT7-19] Toddler-dermal contact with wet preserved materials and mouthing	$AEL_{acute}/_{short\text{-}term}$ = 1	9.4 x 10^{-4}	9.4 x 10^{-2}	Yes
Scenario (screening) Long term inhalation exposure for volatilised active substance	$AEL_{long\text{-}term}$ = 0.37	8.6x10^{-5}	NA	Yes

Preserved film products (PT7)
Based on the predicted exposures and risk characterisation for systemic effects, potential indirect exposures arising from the uses of preserved film products are not considered to pose an unacceptable risk to human health.

Preserved materials (PT9)
There are no indirect exposure scenarios associated with the use of preserved materials (PT9).

Preserved masonry materials (PT10)
There are no indirect exposure scenarios associated with the use of preserved masonry (PT10).

Combined exposure
The predicted combined exposures scenarios calculations for industrial, professional and non-professional workers did not pose an unacceptable risk to human health.
Indirect exposure via food Human exposure to fludioxonil through the diet resulting from its use in biocidal preparations is estimated to be insignificant; it is therefore not necessary to propose or justify acceptable residues.
Fludioxonil is not sprayed/applied on food and feedingstuffs and is unlikely to come into direct contact with food based on its use pattern.
Biocidal preparations of fludioxonil will not be used where food for human consumption is prepared, consumed or stored, or where animal foodstuff is prepared, consumed or stored. Additional studies relating to the behaviour of the residues of active substance, its degradation products, reaction products and metabolites in treated or contaminated foods or foodstuffs are therefore not necessary.
Setting MRLs in food and feedstuffs is not necessary.

SUMMARY OF THE ENVIRONMENTAL RISK ASSESSMENT

Fate and behaviour in the environment

Summary table on relevant physico-chemical and fate and behaviour parameter of fludioxonil			
	Value	**Unit**	**Remarks**
Molecular weight	248.2	g/mol	
Log Octanol/water partition coefficient	4.12	Log 10	Experimental flask method
Organic carbon/water partition coefficient (Koc)	145,600	L/kg	Arithmetic mean, n=5
Henry's Law Constant (20 °C)	2.57×10^{-5}	$Pa/m^3/mol$	Calculated
Biodegradability	Non-biodegrable		Tested in a CO_2 evolution test
DT_{50} for biodegradation in surface water	1326	d (at 12ºC)	Only data from the whole system of a water/sediment degradation test is availbale
DT_{50} for hydrolysis in surface water	stable	d (at 12ºC /pH5, 7 and 9)	No degradation was found in the test
DT_{50} for photolysis in surface water	28	d (at 12ºC)	Highest value of two endpoints
DT_{50} for degradation in soil	502	d (at 12ºC)	Geomean from 8 soils
DT_{50} for degradation in air	6.7	hr (24 hour day)	Estimated value from AOPWIN
DT_{50} for degradation in sediment	no data	d or hr	Only data from the whole system of a water/sediment degradation test is availbale

Calculated fate and distribution in the STP for fludioxonil		
Compartment	**Percentage [%]**	**Remarks**
	Scenario 1 to 4	
Air	2.45×10^{-6}	Calculated with EUSES 2.1.2
Water	12.4	
Sludge	87.6	
Degraded in STP	0	

Summary table on relevant degradation products		
Metabolite/transformation- or reaction product	**Compartment**	**Max formation in compartment (%)[1]**
CGA 339833	Water Soil	30.5 9.1
CGA 344623	Water	12.4
A5	Water	11.5
CGA 192155	Soil	11.7
CGA 265378	Soil	12.3

[1] Highest value among all measurements given in % of applied active substance at test beginning

Summary table on relevant physico-chemical and fate and behaviour parameter of photo-degradation products						
	CGA 339833	**CGA 344623**	**A5**	**CGA 192155**	**CGA 265378**	**Unit**
Molecular weight	312.19	298.2	255.18	202.12	278.17	g/mol
Log Octanol/water partition coefficient[1]	1.68	0.93	2.5-3.3	3.17	3.58	Log 10
Organic carbon/water partition coefficient (Koc)[2]	10	10	22	10	27	L/kg
Henry's Law Constant (25 °C)[3]	6.93×10^{-13}	1.72×10^{-15}	1.14×10^{-8}	5.05×10^{-5}	2.95×10^{-10}	$Pa/m^3/mol$
Biodegradability[4]	No	No	No	No	No	
DT_{50} for biodegradation in surface water	no data					d or hr (at 12ºC)
DT_{50} for hydrolysis in surface water[5]	597	no data				d (at 25ºC /pH7)
DT_{50} for photolysis in surface water	no data					d
DT50 for degradation in soil[5]	30	no data	no data	46	no data	d (at 12ºC)
DT_{50} for degradation in air[6]	9.3	8.1	8.0-8.5	52	20	hr (24 hour day)
DT_{50} for degradation in sediment	no data					d or hr

1 QSAR estimate via KOWWIN v1.68

2 QSAR estimate via KOCWIN v2.00, estimate from MCI method

3 QSAR estimate via HENRYWIN v3.20, estimate from bond method

4 QSAR prediction via BIOWIN v4.10

5 Experimental value

6 QSAR estimate via AOPWIN v1.92

Effects assessment

Summary table on calculated PNEC values for fludioxonil	
Compartment	**PNEC**
Sewage treatment plant (STP)	0.18 mg/L
Freshwater	0.0019 mg/L
Sediment	PNECsediment: 0.40 mg/kg dry sediment (0.0870 mg/kg wet sediment)
Soil	0.00467 mg/kg dwt (0.0369 mg/kg wwt)

In the photo transformation studies in water and soil five relevant photo-transformation products were identified in concentrations above 10% of AR. By using EPIWEB 4.1 QSAR estimates of effect values could be found, these data are shown in Section 4.2-8. By comparing the estimated effect concentrations of the photo-degradation products to the estimated and lowest experimental effect concentrations of fludioxonil it can be concluded that the photo-degradation products are less toxic than fludioxonil and will therefore be covered by the effect assessment of fludioxonil, it is found that this conclusion is applicable for organisms in all the environmental compartments that are assessed. Find the explanation for this in Section 4.2.8.

Exposure assessment

Assessed PT	PT 7: Paints, mineral sealants and silicon coatings – indoor use PT 9: Paper for the manufacturing of drywall/gypsum wallboards – indoor use PT 10: Gypsum central core in drywall boards – indoor use Sporgard WB is used industrially by professional workers in the preparation of treated materials (PT 7, 9 and 10). The end-use treated materials may be used by professionals and non-professionals depending on the particular item.
Assessed scenarios	PT7: Scenario 1: Release estimation from industrial use of biocidal product for manufacture of paint, coatings, mineral sealants and fillers (tonnage approach) Scenario 2a: Release estimation from application and service life from decorative paint (tonnage approach) Scenario 2b: Release estimation from application and service life from sealants (consumption approach) PT9: Scenario 3: Release estimation from manufacture of paper used on drywall/gypsum wallboards (consumption approach) Scenario 4: Release estimation from industrial use of biocidal product for manufacture of paper used on drywall/gypsum wallboards (tonnage approach) PT10: Scenario 5: Release estimation from industrial use of biocidal product for manufacture of gypsum central core in drywall boards (tonnage approach)
ESD(s) used	PT7: Emission Scenario Document for Product Type 7: Environmental Emission Scenarios for Biocides used as Film Preservatives, January 2004 City scenario: Leaching from paints, plasters and fillers applied in urban areas (NL, 2005) PT9: Emission scenario document for biocides used in paper coating and finishing (PT 6, 7 and 9), May 2001 Volume IV, Part B, Appendix 7 – Tonnage based approach – Emission factors for different use categories (A/B – Tables), April 2015
Approach	PT7: Scenario 1: Tonnage based approach (industrial use of biocidal product) Scenario 2a: Tonnage based approach (application and service life of end-use product) Scenario 2a: Consumption based approach (application and service life of end-use product) PT9: Scenario 3: Consumption based approach (manufacture of end-use product)

	Scenario 4: Tonnage based approach (industrial use of biocidal product) PT10: Scenario 5: Tonnage based approach (industrial use of biocidal product)
Distribution in the environment	Calculated based on guidance on the BPR: Volume IV Environment, Part B Risk Assessment (active substance) (Vol. IV, Part B, 2015). Volume IV, Part B, Appendix 7 – Tonnage based approach – Emission factors for different use categories (A/B – Tables), April 2015
Groundwater simulation	Groundwater concentrations for soil photodegradation products were calculated using FOCUS PEARL 4.4.4 (find calculations in the end of the *confidential* appendix)
Confidential Annexes	YES: In the *confidential* Appendix III the tonnage based scenarios 1, 2a, 4 and 5 are provided
Remarks	Tonnage data for the calculation of the release estimation are provided in IUCLID

Summary table on compartments exposed and assessed for PT 7, 9 and 10		
Compartment	**Exposed (Y/N)**	**Assessed (Y/N)**
STP	Y	Y
Surface water	Y	Y
Sediment	Y	Y
Soil	Y	Y
Groundwater	Y	Y
Air	Y	Y

Fludioxonil

In the Table below PEC values are calculated for fludioxonil for the relevant scenarios.

Summary table on calculated PEC values for fludioxonil							
	PEC_{STP} [a]	**PEC_{water}** [a]	**PEC_{sed}** [a]	**$PEC_{soil30d}$** [b]	**$PEC_{soil180d}$** [b] Agr. soil	**PEC_{GW}** [b] Agr. soil	**PEC_{air}** [b]
	[mg/L]	[mg/L]	[mg/kg_{wwt}]	[mg/kg_{wwt}]	[mg/kg_{wwt}]	[µg/l]	[mg/m^3]
PT7							
Industrial use *Scenario 1*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2a*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2b*	1.53×10^{-5}	1.26×10^{-6}	3.98×10^{-3}	1.10×10^{-3}	9.98×10^{-4}	4.31×10^{-4}	1.69×10^{-15}
PT9							
Industrial form. *Scenario 3*	0	0	0	0	0	0	0
Industrial use *Scenario 4*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0	0
PT10							
Industrial use *Scenario 5*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0	0

[a] Predicted environmental concentrations are calculated for the emission episode

[b] Predicted environmental concentrations are calculated for the annual average

Degradation products in water

The major photo-degradation products (>10% applied fludioxonil) in the water phase are identified as CGA 339833 (max. 30.5%), CGA 344623 (max. 12.4%) and A5 (max 11.5%). In the Table below PEC values are calculated for these photo-degradation products in the water and sediment phase.

Summary table on calculated water and sediment PEC values for CGA 339833, CGA 344623 and A5						
	PEC_{water} [a]	**PEC_{sed} [a]**	**PEC_{water} [a]**	**PEC_{sed} [a]**	**PEC_{water} [a]**	**PEC_{sed} [a]**
	[mg/L]	[mg/kg_{wwt}]	[mg/L]	[mg/kg_{wwt}]	[mg/L]	[mg/kg_{wwt}]
PT7	**CGA 339833**		**CGA 344623**		**A5**	
Industrial use *Scenario 1*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2a*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2b*	4.83×10^{-7}	4.83×10^{-7}	1.88×10^{-7}	1.89×10^{-7}	1.49×10^{-7}	1.88×10^{-7}
PT9						
Industrial form. *Scenario 3*	0	0	0	0	0	0
Industrial use *Scenario 4*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0
PT10						
Industrial use *Scenario 5*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0
[a] Predicted environmental concentrations are calculated for the emission episode						

Degradation products in soil

The major photo-degradation products (>10% applied fludioxonil) in the soil phase are identified as CGA 339833 (max. 9.1%), CGA 192155 (max. 11.7%) and CGA 265378 (max 12.3%). In the Table below PEC values are calculated for these photo-degradation products in the soil and groundwater phase.

Summary table on calculated water and sediment PEC values for CGA 339833, CGA 192155 and CGA 265378						
	$PEC_{soil30d}$ [b]	**PEC_{GW}** [b] Agr. soil	**$PEC_{soil30d}$** [b]	**PEC_{GW}** [b] Agr. soil	**$PEC_{soil30d}$** [b]	**PEC_{GW}** [b] Agr. soil
	[mg/kg_{wwt}]	[µg/l]	[mg/L]	[mg/kg_{wwt}]	[mg/L]	[mg/kg_{wwt}]
PT7	**CGA 339833**		**CGA 192155**		**CGA 265378**	
Industrial use *Scenario 1*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2a*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2b*	1.26×10^{-4}	0.43	1.05×10^{-4}	0.36	1.52×10^{-4}	0.26
PT9						
Industrial form. *Scenario 3*	00	0	0	0	0	0
Industrial use *Scenario 4*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0
PT10						
Industrial use *Scenario 5*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0

[b] Predicted environmental concentrations are calculated for the annual average

As a number of the soil photodegradation products were calculated to be greater than the regulatory limit of 0.1 µg/L in groundwater, further modelling was conducted using the groundwater model FOCUS PEARL 4.4.4. An application rate for soil was calculated from the aggregated soil concentration for each metabolite.[2]

The PECs calculated for groundwater are presented in the table below.

Summary of FOCUS PEARL calculated groundwater PECs for CGA339833, CGA192155 and CGA265378			
Scenario	**80th percentile PECgw (µg/L)**		
	CGA339833	**CGA192155**	**CGA265378**
	PEARL	**PEARL**	**PEARL**
Châteaudun	<0.1	<0.1	<0.1
Hamburg	<0.1	**>0.1**	**>0.1**
Jokioinen	<0.1	**>0.1**	**>0.1**
Kremsmünster	<0.1	**>0.1**	**>0.1**
Okehampton	**>0.1**	**>0.1**	**>0.1**
Piacenza	<0.1	**>0.1**	**>0.1**
Porto	**>0.1**	**>0.1**	**>0.1**
Sevilla	<0.1	<0.1	<0.1
Thiva	<0.1	<0.1	<0.1

2 New calculations are made for the exposure calculations, however for the modelling of groundwater concentrations using FOCUS PEARL former values are used. These are worst case compared to the new calculations. New modelling of groundwater concentrations has not been performed as a safe risk was obtained for at least three of the scenarios.

Risk characterization

In the Table below PEC/PNEC values are calculated for fludioxonil for the relevant scenarios.

Summary table on calculated PEC/PNEC values for fludioxonil					
	PEC/PNEC$_{STP}$	**PEC/PNEC$_{water}$**	**PEC/PNEC$_{sed}$**	**PEC/PNEC$_{soil30d}$**	**PEC$_{GW}$/max limit** Agr. soil
PT7					
Industrial use *Scenario 1* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *Scenario 2a* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *Scenario 2b* *Consumption*	8.25×10^{-5}	6.63×10^{-4}	0.0457	0.0299	4.31×10^{-3}
PT9					
Industrial form. *Scenario 3* *Consumption*	0	0	0	0	0
Industrial use *Scenario 4* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *No emission*	0	0	0	0	0
PT10					
Industrial use *Scenario 5* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0

Private use and service life *No emission*	0	0	0	0	0
Aggregated risk					
Aggregated risk	<1.0	<1.0	<1.0	<1.0	<1.0

Degradation products in water

The major photo-degradation products (>10% applied fludioxonil) in the water phase are identified as CGA 339833 (max. 30.5%), CGA 344623 (max. 12.4%) and A5 (max 11.5%). In the Table below PEC/PNEC values are calculated for these photo-degradation products in the water and sediment phase. PNEC values for fludioxonil are used as a worst case.

Summary table on calculated water and sediment PEC/PNEC values for CGA 339833, CGA 344623 and A5						
	$PEC/PNEC_{water}$	**$PEC/PNEC_{sed}$**	**$PEC/PNEC_{water}$**	**$PEC/PNEC_{sed}$**	**$PEC/PNEC_{water}$**	**$PEC/PNEC_{sed}$**
PT7	**CGA 339833**		**CGA 344623**		**A5**	
Industrial use *Scenario 1* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *Scenario 2a* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *Scenario 2b* *Consumption*	2.54×10^{-4}	5.56×10^{-6}	9.88×10^{-5}	2.18×10^{-6}	7.84×10^{-5}	2.16×10^{-6}
PT9						
Industrial form. *Scenario 3* *Consumption*	0	0	0	0	0	0
Industrial use	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0

Scenario 4 *Tonnage*						
Private use and service life *No emission*	0	0	0	0	0	0
PT10						
Industrial use *Scenario 5* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *No emission*	0	0	0	0	0	0
Aggregated risk						
Aggregated risk	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0

Degradation products in soil

The major photo-degradation products (>10% applied fludioxonil) in the soil phase are identified as CGA 339833 (max. 9.1%), CGA 192155 (max. 11.7%) and CGA 265378 (max 12.3%). In the Table below PEC/PNEC values are calculated for these photo-degradation products in the soil and groundwater phase. The PNECsoil value for fludioxonil is used as a worst case. For groundwater the max limit of 0.1 µg/L is applied.

Summary table on calculated soil and refined groundwater PEC/PNEC values for CGA 339833, CGA 192155 and CGA 265378						
	$PEC/PNEC_{soil30d}$	**PEC_{GW}/max limit** Agr. soil	**$PEC/PNEC_{soil30d}$**	**PEC_{GW}/max limit** Agr. soil	**$PEC/PNEC_{soil30d}$**	**PEC_{GW}/max limit** Agr. soil
PT7	**CGA 339833**		**CGA 192155**		**CGA 265378**	
Industrial use *Scenario 1*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *Scenario 2a*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0

Private use and service life *Scenario 2b*	3.42 x 10^{-3}	<1.0	2.85 x 10^{-3}	<1.0	4.12 x 10^{-3}	<1.0
PT9						
Industrial form. *Scenario 3* *Consumption*	0	0	0	0	00	0
Industrial use *Scenario 4* Tonnage	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *No emission*	0	0	0	0	0	0
PT10						
Industrial use *Scenario 5* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *No emission*	0	0	0	0	0	0
Aggregated risk						
Aggregated risk	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0

Conclusion:
Atmosphere: Fludioxonil has a low vapour pressure of 3.9 x 10^{-7} Pa (at 25ºC) and a low Henry's law constant of 5.4 x 10^{-5} m^3 Pa mol^{-1}. Therefore, volatilisation from soil or water is not expected to be a significant entry route into air for fludioxonil. Based on Atkinson calculation at standard conditions (5 x 10^5 OH radicals/cm^3, 24 hour day) the photochemical oxidative degradation in air would proceed with a half-live of 6.7 hours (3.6 hours for a 12 hour day, 1.5 x 10^6 OH radicals/cm^3). Referring to these results, an accumulation of fludioxonil in air is not expected.

For the sewage treatment plant, freshwater and soil compartment the requirements for acceptable risk are met for all the single uses of fludioxonil (covering also the degradation products) as well as for the aggregated risk.

Groundwater: Fludioxonil has a very high Koc and is very unlikely to reach the groundwater compartment. The porewater values calculated are below 0.1 µg/L and as such indicate no risk to groundwater.
The soil photodegradation products, CGA339833, CGA192155 and CGA265378 have low Koc values and were calculated to occur in groundwater at above 0.1 µg/L. However, higher tier modelling of the degradation products was conducted with FOCUS PEARL 4.4.4, which indicated that the photodegradation products would not occur in groundwater at levels above 0.1 µg/L in a number of scenarios. Consequently, no risk to groundwater is expected.

Primary and secondary poisoning: No primary poisoning is foreseen for the product.
According to the guidance (REACH R16, point R16.6.7), a detailed assessment of secondary poisoning is required if a substance has a bioaccumulation potential, and is neither readily biodegradable nor hydrolysable, and may also cause toxic effects if accumulated in higher organisms. Based on this assessment, consideration of the secondary poisoning exposure route is not found relevant for fludioxonil.

The aggregated risk was evaluated by a simple addition of PEC/PNEC values for all scenarios, both tonnage and consumption based approaches. For all environmental compartments no unacceptable risk is found.
When considering the treated article, gypsum plates, then both PT9 and PT10 uses are included in the final treated article. It could therefore be argued that PT9 and PT10 should be evaluated together. When considering PT9 and PT10 together by adding PEC/PNEC values from scenario 4 with those for scenario 5 then a safe risk is found.

3 ASSESSMENT OF EXCLUSION, SUBSTITUTION CRITERIA AND POP

Conclusion on exclusion criteria	The exclusion criteria in BPR Article 5(1)a-e are not met.
Conclusion on CMR	The exclusion criteria in BPR Article 5(1)a-c are not met.
Conclusion on ED assessment	The exclusion criteria in BPR Article 5(1)d are not met. Therefore, the interim criteria for endocrine disruptors are not met.
Conclusion on PBT and vP/vB criteria	Fludioxonil is not a PBT / vPvB substance, however fludioxonil fulfils the criteria for being vP. The photo-degradation products are vP based on QSARs.

Conclusion on substitution criteria	Fludioxonil does not meet the conditions laid down in Article 10 of Regulation (EU) No 528/2012. Fludioxonil is therefore not considered as a candidate for substitution.

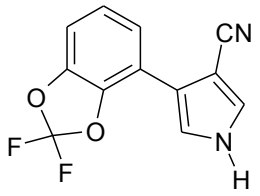
Conclusion on LRTAP/POP assessment	Fludioxonil fulfils the criteria for being vP. However fludioxonil does not demonstrate the potential for long range transport. In view of this, fludioxonil does not meet the criteria for being a persistent organic pollutant. The photo-degradation products are vP based on QSARs. None of the substances demonstrate potential for long range transport. The substances do therefore not fulfil the criteria for being persistent organic pollutants.

Part A Assessment of intrinsic properties and effects of the active substance

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

Summary table on substance identity	
Common name (ISO name, synonyms)	Fludioxonil
Chemical name (EC name, CA name, IUPAC name	4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1H-pyrrole-3-carbonitrile
EC number	Not allocated
CAS number	131341-86-1
other CAS numbers (e.g. deleted, related, preferred, alternate)	1135442-63-5 (deleted)
Molecular formula	$C_{12}H_6F_2N_2O_2$
SMILES notation	c12OC(F)(F)Oc2cccc1C3=CNC=C3C#N
Molar mass	248.2 g/mol

Structural formula


Origin of the natural active substance or precursor(s) of the active substance
-

Method of manufacture
This information is confidential, please refer to annex VI in the CAR and IUCLID section 2.8 for further information

1.2 COMPOSITION OF THE SUBSTANCE (REFERENCE SPECIFICATIONS)

Main constituent(s)			
Constituent (chemical name)	**Typical concentration (%(w/w))**	**Concentration range (%(w/w))**	**Remarks / Discussion**
Fludioxonil; (4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1H-pyrrole-3-carbonitrile)	95	-	-

Relevant impurities			
Constituent (chemical name)	**Typical concentration (%(w/w))**	**Concentration range (%(w/w))**	**Remarks / Discussion**
sodium 4-toluene sulphonate (SYN549410)	Max. 5 g/kg	**-**	**Environmental relevant**
1-[2-cyano-1-(2,2-difluoro-1,3-benzodioxol-4-yl)ethyl]-4-(2,2-difluoro-1,3-benzodioxol-4-yl)pyrrole-3-carbonitrile (SYN549129)	Max. 1 g/kg	**-**	**Toxicological relevant**

Please refer to the confidential section in annex VI for a summary of the reference specification and the (eco)toxicological studies, including the two relevant impurities SYN549410 and SYN549129.

1.3 PHYSICAL AND CHEMICAL PROPERTIES OF THE ACTIVE SUBSTANCE

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Aggregate state at 20°C and 101.3 kPa	See physical state (appearance) results below			
Physical state (appearance) at 20°C and 101.3 kPa	Powder	Visual. Temperature: not documented	Batch [redacted], [redacted] TGAI. GLP study. Reliability 1.	Rodler, M., 1992 (IUCLID 3.1-01)
	Fine powder	Visual. Temperature: 25ºC	Batch [redacted], [redacted]. GLP study. Reliability 1.	Das, R., 1998 (IUCLID 3.1-02)
Colour at 20°C and 101.3 kPa	Light olive green	Visual. Temperature: not documented	Batch [redacted], [redacted]. GLP study. Reliability 1.	Rodler, M., 1992 (IUCLID 3.2-01)
	Faintly yellow	Visual. Temperature: 25ºC	Batch [redacted], [redacted]. GLP study. Reliability 1.	Das, R., 1998 (IUCLID 3.1-02)
Odour at 20°C and 101.3 kPa	Odourless	Organoleptic. Temperature: not documented	Batch [redacted], [redacted] TGAI. GLP study. Reliability 1.	Rodler, M., 1992 (IUCLID 3.2-01)
	Odourless	Organoleptic. Temperature: 25ºC	Batch [redacted], [redacted]. GLP study. Reliability 1.	Das, R., 1998 (IUCLID 3.1-02)
Melting / freezing point	199.8°C	EEC A.1 (≡ OECD 102). Differential scanning calorimetry (DSC analysis)	Batch [redacted], [redacted]. GLP study. Reliability 1.	Rodler, M., 1992 (IUCLID 3.1-01)
Acidity, alkalinity	Fludioxonil is poorly soluble in water. The applicant has stated that fludioxonil does not dissociate or associate in water and has no acidic or basic functional groups that would create significant acidity (pH <4) or alkalinity (pH > 10) in aqueous solution. pH outside the range that would require acidity or alkalinity to be measured is not expected and it is not considered necessary to conduct a study to measure these parameters. This justification is accepted.			

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Boiling point at	Not determined since thermal decomposition starts at about 306°C	EEC A.2 (≡ OECD 103). Test conducted at 23ºC	Batch [redacted], [redacted]. GLP study. Reliability 1.	Das, R., 2000 (IUCLID 3.4-01)
Relative density	Bulk density = 1.54 x 10^3 kg/m^3 corresponding to a relative density of 1.54	OECD 109 (≡ EEC A.3)	Batch [redacted], [redacted]. GLP study. Reliability 1.	Füldner, H., 1992 (IUCLID 3.5-01)
Absorption spectra data (UV/VIS, IR, NMR) and a mass spectrum, molar extinction coefficient at relevant wavelengths, where relevant	The molar extinction coefficient [l/mol · cm] were determined to be: Neutral solution: 12384 (λ_{max} = 266 nm) Acidic solution: 12327 (λ_{max} = 265 nm) Basic solution: 11790 (λ_{max} = 271 nm) No absorption maximum between 340 and 750 nm	UV/VIS Methanol OECD 101	Batch [redacted], [redacted]. GLP study. Reliability 1.	Stulz, J., 1998 (IUCLID 3.6-01)
	1236 cm^{-1} (C-F strength), 1652, 1530 cm^{-1} (aromatic skeletons vibrations), 2223 cm^{-1} (CN stretch), 3289 cm^{-1} (N-H stretch)	IR KBr pellet		
	Spectrum is consistent with the structure of the active substance	^{1}H-NMR DMSO		
	Molecular peaks at m/z: 127, 154, 182 and 248 (molecular ion) All spectra are consistent with the structure of the active substance	MS EI		
	Spectrum is consistent with the structure of the active substance	^{13}C-NMR DMSO	Batch [redacted], [redacted]. GLP study. Reliability 1.	Stulz, J., 1998 (IUCLID 3.6-02)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Vapour pressure	Temperature: 25ºC 3.9 x 10^{-7} Pa (extrapolated) Vapour pressure curve: ^{10}log P [Pa] = 16.8495 - 6936.15 x 1/T [K]	EEC A.4 (≡OECD 104). Gas saturation method	Batch [redacted], [redacted]. GLP study. Reliability 1.	Rordorf, B., 1992 (IUCLID 3.7.1-01)
Henry's law constant	Measured/calculated: 5.4 x 10^{-5} Pa m³/mol	Calculation. Calculated at 25 ºC from the water solubility and vapour pressure determinations	-	Burkhard, N., 1994 (IUCLID 3.7.2-01)
Surface tension	47.7 - 48.5 mN/m (plate method applied to filtrates of 10 g/l suspension, concentration 1.8 mg/L, 100% saturated solution) Temperature: 20ºC The test was conducted at 100% concentration for solubility whereas the guidance indicates that the test should be performed at 90% concentration at maximum. As the structure of the compound does not indicate any surface activity. The test is therefore considered false positive, possibly due to interaction with residual undissolved substance, and based on the structure of the compound fludioxonil is not considered surface active. No new tests are required to support this.	OECD 115 (≅ EEC A.5).	Batch [redacted], [redacted] GLP study. Reliability 3.	Ryser, M., 1992 (IUCLID 3.8-01)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Water solubility	1.8 mg/l pH: Fludioxonil has no dissociation within the range pH 2 to pH 12, that means the pH has no effect on the water solubility of the compound in the pH range 5 to 9 The solubility is low and therefore effects of temperature and pH are not expected to be significant. Solubility results at each centrifugation speed (30000, 40000 and 50000 G) are within the OECD 105 guideline acceptance criteria for the flask method (RSD <15%) indicating that solubility is measured with sufficient accuracy using this method. Actual solubility measurements at the three centrifugation speeds are 2.04 (5.4% RSD), 1.77 (7.6% RSD) and 1.66 mg/L (2.7% RSD), respectively, with a mean of 1.83 mg/L (10.4% RSD). Although the solubility appears to be decreasing this is not the case for all replicates and the overall standard deviation is within the guideline	OECD 105 (≡ EEC A.6). Temperature: 25ºC	Batch [redacted], [redacted]. GLP study. Reliability 2. The applicants justification regarding effects of temperature and pH is accepted.	Rodler, M., 1992 (IUCLID 3.9-01)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
	recommendation.			
Partition coefficient (n-octanol/water) and its pH dependency	log Pow = 4.12 ± (0.016) pH: Fludioxonil has no dissociation within the range pH 2 to pH 12, that means the pH has no effect to partition coefficient of the compound in the pH range 5 to 9	OECD 107 (≡ EEC A.8). Temperature: 25ºC	Batch [redacted], [redacted]. GLP study. Reliability 1. The shake-flask method can be used within the range of log Pow –2 to 4 (occasionally up to 5) and though the result is very close to the upper limit it is accepted. Fludioxonil is surface active but the test and result is acceptable as it is described in the study that aliquots from the clear, separated octanol and aqueous phases were analysed. [redacted]	Rodler, M., 1992 (IUCLID 3.10-01)
Thermal stability and identity of breakdown products	Thermal decomposition starts at about 306°C	EEC A.2 (≡ OECD 103). DSC analysis	Batch [redacted], [redacted] GLP study. Reliability 1.	Das, R., 2000 (IUCLID 3.11-02)
	No thermal effect found between room temperature and 150°C	OECD 113	Batch [redacted], [redacted] GLP study. Reliability 1.	Schürch, H., 1992 (IUCLID 3.11-01)
Reactivity towards container material	Fludioxonil is stable when stored in polypropylene bags for up to 2 years at 25°C. No effects on the container material have been reported.	In house	Batch [redacted], [redacted] GLP study. Reliability 1.	Kettner, R., 2005 (IUCLID 3.12-01)
Dissociation constant	The estimated dissociation constants of fludioxonil in water were found to be:	OECD 112. Spectrophotometric titration method was selected due to low aqueous solubility	Batch [redacted], [redacted]. GLP study. Reliability 1.	Jäkel, K., 1992 (IUCLID 3.13-01)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
	pK_{a1} < 0 (basic) pK_{a2} ~14.1 (acidic)			
Granulometry	Median: 46.6 µm % undersize d(10): 17.8 µm % undersize d(90): 90.1 µm	CIPAC 187	Batch [redacted], [redacted]. GLP study. Reliability 1.	Das, R., 2009 (IUCLID 3.14-01)
Viscosity	Not applicable because the active substance is a solid.			
Solubility in organic solvents, including effect of temperature on solubility	Acetone: 190 g/l Dichloromethane: 7.3 g/l Ethyl acetate: 86 g/l Hexane: 10 mg/l Methanol: 42 g/l Octanol: 20 g/l Toluene: 2.7 g/l	CIPAC MT 157.3. Saturation method, analysis by HPLC/UV Temperature: 25ºC	Batch [redacted], [redacted]. GLP study. Reliability 1.	Kettner, R., 2000 (IUCLID 3.16-01)
Stability in organic solvents used in biocidal products and identity of relevant degradation 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.			

1.4 PHYSICAL HAZARDS AND RESPECTIVE CHARACTERISTICS

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Explosives	Not explosive	EEC A.14	Batch [redacted], [redacted]. GLP study. Reliability 1.	Schürch, H., 1992 (IUCLID 4.1-01)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Flammable gases	Not applicable, the active substance is a solid.			
Flammable aerosols	Not applicable, the active substance is a solid.			
Oxidising gases	Not applicable, the active substance is a solid.			
Gases under pressure	Not applicable, the active substance is a solid.			
Flammable liquids	Not applicable, the active substance is a solid.			
Flammable solids	Fludioxonil is not considered highly flammable	EEC A.10 (Flammability of solids)	Batch [redacted], [redacted] GLP study. Reliability 3. Flammability is not tested in accordance to EEC A.10. The ignition source should be a flame not a hot platinium wire. Study not accepted for the end point. Instead refer to Jackson, 2004.	Schürch, H., 1992 (IUCLID 4.2-01)
	Fludioxonil is not considered highly flammable	EEC A.10 (Flammability of solids)	Batch [redacted], [redacted] GLP study. Reliability 1.	Jackson, W.A., 2004 (IUCLID 4.2-02)
Self-reactive substances and mixture	The active substance is neither flammable, explosive nor oxidising. The active substance is a stable organic molecule with no functional groups that indicate a hazard for self-reaction. No incidences of self-reaction have occurred during manufacture and extensive use of the active substance. The active substance is not a self reacting substance.			
Pyrophoric liquids	Not applicable, the active substance is a solid.			
Pyrophoric solids	The active substance is neither flammable, explosive nor oxidising. The active substance is a stable organic molecule with no functional groups that indicate a pyrophoric hazard. No incidences of self-ignition have occurred during manufacture and extensive use of the active substance. The active substance is not a pyrophoric solid.			
Self-heating substances and	The active substance is neither flammable, explosive nor oxidising.			

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
mixtures	The active substance is a stable organic molecule with no functional groups that indicate a hazard for self-heating. No incidences of self-heating have occurred during manufacture and extensive use of the active substance. The active substance is not a self heating substance.			
Substances and mixtures which in contact with water emit flammable gases	The active substance is used in aqueous formulations and does not emit flammable gas in contact with water.			
Oxidising liquids	Not applicable, the active substance is a solid.			
Oxidising solids	Not oxidising	EEC A.17	Batch [redacted], [redacted] GLP study. Reliability 1.	Schürch, H., 1992 (IUCLID 4.4-01)
Organic peroxide	Not applicable, the active substance contains no organic peroxides.			
Corrosive to metals	The active substance is neither flammable, explosive nor oxidising. The active substance is a stable organic molecule with no functional groups that infer strongly acidic or basic properties. No incidences of damage to metals have occurred during manufacture and extensive use of the active substance. The active substance is not considered to be corrosive to metals.			
Auto-ignition temperature (liquids and gases)	Not applicable, the active substance is a solid.			
Relative self ignition temperature for solids	Not auto-flammable. No auto-ignition temperature	EEC A.16 (Auto-ignition)	Batch [redacted], [redacted]. GLP study. Reliability 1.	Schürch, H., 1992 (IUCLID 4.17.1-02)
Dust explosion hazard	Fludioxonil active substance is handled in closed systems and in low amounts. A build up of dust is not expected due to engineering controls during manufacture and handling of the substance. The formation of a hazardous dust atmosphere is not expected.			

1.5 HAZARD IDENTIFICATION FOR PHYSICO-CHEMICAL PROPERTIES

The technical grade a.s. is an odourless light olive green powder ([redacted]) while the pure a.s is an odourless faintly yellow fine powder ([redacted]). The vapour pressure is low at 3.9 x 10^{-7} Pa at 25ºC.

Fludioxonil is considered a surface active substance at 20 ºC with a surface tension of 47.7 - 48.5 mN/m.

Solubility in water is low at 1.8 mg/l. The solubility is considered independent of temperature and pH in the interval of pH 5 to 9 due to no dissociation in this range.

Fludioxonil has a partition coefficient of log Pow = 4.12 and a Henry's law constant of 5.4 x 10^{-5} Pa m³/mol (Calculated at 25 ºC).

Fludioxonil is not considered highly flammable, explosive, oxidising or auto-flammable and should not be classified for physic-chemical properties.

1.6 ANALYTICAL METHODS FOR DETECTION AND IDENTIFICATION

Analytical methods								
Analyte (type of analyte e.g. active substance, metabolite etc.)	**Compartment**	**Linearity**	**Specificity**	**Recovery rate (%)**			**Limit of quantification (LOQ), Maximum Residue Limits or other limits**	**Reference**
				Fortification range / Number of measurements	Mean	RSD		
Fludioxonil (technical material, TC)	-	The linearity was tested using 5 concentrations of fludioxonil in the range of 50% to 150% of the target level. r^2 = 0.99960	There are no known substances which would interfere with the detection of the analyte.	-	Not determined for the technical material.	The relative standard deviation from 5 replicates was calculated as 0.59%.	The limit of quantification is not relevant for the active substance.	Tomann, A., 1992 (IUCLID 5.1-01, -02)

Fludioxonil	Sandy Loam (Pappelacker Soil)	A typical calibration curve has been presented over the range 0.0001 to 0.01 µg/mL (4 pg to 0.4 ng). 5 samples each measured in triplicate. The correlation coefficient was determined to be 0.9993.	There are no substances which would interfere with the detection of fludioxonil.	0.01 mg/kg (n=5)	86	1	The limit of quantification of the method is the lowest analyte concentration in a sample which the methodology has been validated. The LOQ for this procedure is estimated to be 0.01 mg/kg.	Robinson, N.J. and Tummo n, O.J., 2004 (IUCLID 5.2.1-01)
				0.10 mg/kg (n=5)	86	3		
				1.5 mg/kg (n=5)	92	3		
	Silty Clay Loam (Scheueracker soil)			0.01mg/kg (n=15)	83	4		
				0.10 mg/kg (n=5)	81	2		
				1.5 mg/kg (n=5)	92	3		
	BBA 2.2 (Soil type 1)	A typical calibration curve has been presented over the range 0.05 to 10 µg/L. 8 samples each measured. The correlation coefficient was determined to be 0.9994-0.9996.	There are no known substances which would interfere with the detection of fludioxonil. Confirmation is by an additional transition.	0.01 mg/kg (n=5)	Primary transition: 100 Confirmatory transition: 99	Primary transition: 5.4 Confirmatory transition: 5.8	The limit of quantification has been set at 0.01 mg/kg.	Braid, S., 2015 and Hamberger, R., 2015 (IUCLID 5.2.1-02)
				0.1 mg/kg (n=5)	Primary transition: 95 Confirmatory transition: 94	Primary transition: 1.7 Confirmatory transition: 1.2		

				Overall (n=10)	Primary transition: 97 Confirmatory transition: 96	Primary transition: 4.6 Confirmatory transition: 5.1		
	BBA 5M (Soil type 2)			0.01 mg/kg (n=5)	Primary transition: 100 Confirmatory transition: 98	Primary transition: 3.8 Confirmatory transition: 3.0		
				0.1 mg/kg (n=5)	Primary transition: 96 Confirmatory transition: 94	Primary transition: 1.4 Confirmatory transition: 1.3		
				Overall (n=10)	Primary transition: 98 Confirmatory transition: 96	Primary transition: 3.4 Confirmatory transition: 3.3		

Fludioxonil	Air (Indoor, 22°C, 29% RH)	Not reported.	There are no substances which would interfere with the detection of fludioxonil. Confirmation is by reversed phase HPLC.	10 μg/m^3 (n=1)	86	3.8 (n=3)	The limit of quantification is 10 µg/m3 (defined as the lowest concentration at which acceptable recovery has been demonstrated).	Tribolet, R., 1992 (IUCLID 5.2.2-01)
				20 μg/m^3 (n=1)	92			
				100 μg/m^3 (n=1)	92			
	Air (Outdoor, 8°C, 64% RH)			10 μg/m^3 (n=1)	86	4.7 (n=3)		
				20 μg/m^3 (n=1)	88			
				100 μg/m^3 (n=1)	94			
	Air (35°C, 80% RH)			2 μg/m^3 (n=8)	96	1.4	The limit of quantification is 2 µg/m3 (defined as the lowest concentration at which acceptable recovery has been demonstrated).	Tribolet, R., 1996 (IUCLID 5.2.2-02)
				50 μg/m^3 (n=8)	93	1.0		
				10-100 μg/m^3 (n=6)	90	3.8		
	Air (confirmatory method, reverse phase)	A typical calibration curve has been presented over the range 0.1 to 1.2 µg/m^3 (5 to	There are no known substances which would interfere with the detection of	2 μg/m^3 (n=3)	92	1.9	The limit of quantification is 2 µg/m3 (defined as the lowest concentration at which acceptable recovery has been	Tribolet, R., 2001 (IUCLID 5.2.2-03)

		60 ng). Ten measurements. Correlation coefficient r^2 = 0.9997.	fludioxonil.	50 μg/m^3 (n=3)	94	5.3	demonstrated).	
Fludioxonil and the metabolites CGA192155 and CGA339833	River water	A typical calibration curve has been presented over the range 0.1 to 50 µg/mL (1 pg to 500 pg). Standards at 7 different concentration level injected in triplicate. The linearity of the detector response (LC-MS/MS) was confirmed by plotting a graph of mean response plotted against amount injected. The intercept was set to zero and the linear trend fit applied. The	There are no known substances which would interfere with the detection of fludioxonil. Confirmation is by an additional transition.	FLU, primary transition	-	-	The limit of quantification of the method is defined as the lowest analyte concentration in a sample at which the methodology has been validated. The limit of quantification has been set at 0.05 µg/L for both the primary and confirmatory method. The limit of determination for **fludioxonil** in river water, groundwater and drinking water was estimated to be 0.00019-0.00053 µg/L using the primary transition and between 0.0011-0.0045 µg/L using the confirmatory	Robinson, N.J., 2007 Nagra, B.S., 2007 (IUCLID 5.2.3-01, -02)
				0.05 mg/kg (n=5)	101	2		
				0.5 mg/kg (n=5)	94	4		
				FLU, confimatory transition	-	-		
				0.05 mg/kg (n=5)	102	3		
				0.5 mg/kg (n=5)	95	4		
				CGA192155, primary transition	-	-		
				0.05 mg/kg (n=5)	98	2		
				0.5 mg/kg (n=5)	95	2		

		correlation coefficient was determined to be >0.9992 for all mass transitions.		CGA192155, confimatory transition	-	-	transition. The limit of determination for **CGA192155** in river water, groundwater and drinking water was estimated to be 0.00051-0.00080 µ/L using the primary transition and between 0.0015-0.0066 µg/L using the confirmatory transition. The limit of determination for **CGA339833** in river water, groundwater and drinking water was estimated to be 0.0031-0.010 µg/L using the primary transition and between 0.0052-0.0079 µg/L using the confirmatory transition.	
				0.05 mg/kg (n=5)	95	2		
				0.5 mg/kg (n=5)	94	1		
				CGA339833, primary transition	-	-		
				0.05 mg/kg (n=5)	107	3		
				0.5 mg/kg (n=5)	109	1		
				CGA339833, confimatory transition	-	-		
				0.05 mg/kg (n=5)	99	6		
				0.5 mg/kg (n=5)	110	2		
	Groundwater			FLU, primary transition	-	-		
				0.05 mg/kg (n=5)	101	5		
				0.5 mg/kg (n=5)	98	5		

				FLU, confimatory transition	-	-		
				0.05 mg/kg (n=5)	100	4		
				0.5 mg/kg (n=5)	97	5		
				CGA192155, primary transition	-	-		
				0.05 mg/kg (n=5)	100	3		
				0.5 mg/kg (n=5)	96	2		
				CGA192155, confimatory transition	-	-		
				0.05 mg/kg (n=5)	98	2		
				0.5 mg/kg (n=5)	96	2		
				CGA339833, primary transition	-	-		
				0.05 mg/kg (n=5)	81	2		
				0.5 mg/kg (n=5)	85	18		

				CGA339833, confimatory transition	-	-		
				0.05 mg/kg (n=5)	81	15		
				0.5 mg/kg (n=5)	86	17		
	Drinking water			FLU, primary transition	-	-		
				0.05 mg/kg (n=5)	99	6		
				0.5 mg/kg (n=5)	98	4		
				FLU, confimatory transition	-	-		
				0.05 mg/kg (n=5)	100	4		
				0.5 mg/kg (n=5)	99	4		
				CGA192155, primary transition	-	-		
				0.05 mg/kg (n=5)	92	2		
				0.5 mg/kg (n=5)	94	4		

				CGA192155, confimatory transition	-	-		
				0.05 mg/kg (n=5)	94	4		
				0.5 mg/kg (n=5)	92	3		
				CGA339833, primary transition	-	-		
				0.05 mg/kg (n=5)	88	13		
				0.5 mg/kg (n=5)	87	6		
				CGA339833, confimatory transition	-	-		
				0.05 mg/kg (n=5)	91	15		
				0.5 mg/kg (n=5)	88	7		

Summary of analytical methods

Method for determination of the active substance as manufactured
The determination of the active substance, fludioxonil, was carried out using high performance liquid chromatography on a reversed phase C18 column using a linear gradient program and UV detection at 270 nm. Quantification was achieved by comparison of peak area with an external standard.

Recovery has not been reported for the method. This is however acceptable as it is not a requirement when the method is performed on the technical material (TC). As a specific analytical method is used for the determination of the active substance as manufactured, comfirmation of the method is not required. The method is considered validated.

Method for determination of impurities in the technical active substance as manufactured
The analytical method for the determination of impurities in the active substance as manufactured is confidential. This information is provided separately in the confidential part of the CAR, annex 6. For further information please also refer to IUCLID section 5.1-04, -04.

Method on soil
In the method by Robinson, N.J. and Tummo n, O.J., 2004 (IUCLID 5.2.1-01), soil is extracted by shaking with methanol/water (90:10, v/v) followed by centrifugation. The supernatant is decanted and the extraction repeated with further methanol/water (90:10, v/v). The extracts are combined and made up to a 100 mL volume and addition of water and sodium chloride solution. Determination is by HPLC using a Kromasil KR100 ODS 5 µm with acetonitrile/0.2% acetic acid in water mobile phase (gradient) with a mass spectrometer for detection (API, negative mode, Q1: 247.0 and Q3: 179.9).

The method has been developed for two different types of soil compartments, Sandy Loam and Silty Clay Loam. The method has been validated and audited as a GLP study (Robinson, 2004) for fludioxonil. The detector response is linear for five reference standards within the concentration range from 0.0001 to 0.01 µg/mL. No interferences were observed. LOQ is below the PNECsoil value of 0.0369 mg/kg (LOQ = 0.01 mg/kg). No confirmatory data has been submitted for this method and it is therefore not regarded as acceptable by CA DK.

However, a second method on soil was submitted by the applicant.
In the method by Braid, S., 2015 and Hamberger, R., 2015 (IUCLID 5.2.1-02) samples of soil are extracted with methanol/water (90/10, v/v) using mechanical agitation. Samples are centrifuged and diluted with water. Final determination is by high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS).
Two transitions are monitored; primary transition m/z 247 to 180 and confirmatory transition m/z 247 to 126.

The method has been validated and audited as a GLP study (Braid, S., 2015 and Hamberger, R., 2015) for fludioxonil in two types of soil. No interferences were observed. The detector response is linear for eight reference standards within the concentration range from 0.05 to 10 µg/L. Confirmation simulteaneously to the primary detection of fludioxonil has been

performed by using an additional transition for the LC-MS/MS detection (QTRAP, negative mode).

The stability of fludioxonil in control soil samples (methanol/water (90:10 v/v), diluted 1:3 (v/v) with HPLC water) was tested by storage of the samples at a temperature between 2 and 8 °C for a period of 7 days. The samples were then re-analysed against freshly prepared non-matrix calibration standards. No significant degradation of fludioxonil in final soil extracts was observed when stored under the specified conditions.

LOQ for both the primary and confirmatory method is 0.01 mg/kg and is thus below the PNECsoil value of 0.0369 mg/kg wwt. This method is therefore regarded as acceptable by CA DK.

Method on air

A defined volume of air is sucked through a sorbent tube using an air sampler pump. The different layers of the tube are separated and fludioxonil (CGA 173506) is extracted with methanol using an ultrasonic bath. The methanol is evaporated and the residue is re-dissolved in mobile phase. Fludioxonil is determined by high performance liquid chromatography (HPLC) using a UV (268 nm) detector.
Confirmatory method: Reversed phase HPLC using a two-column switching system, Inertsil Phenyl and Nucleosil C18 columns with acetonitrile/water (50:50 v/v) and acetonitrile/water (60:40 v/v) mobile phases. Detector: UV/VIS (268 nm).

It is assessed that the validation data for the method described in Tribolet 1992 and 1996 is not acceptable as the linearity of the method is not described. A validated confirmatory method has however been submitted, where the detector response is linear for four reference standards within the concentration range from 0.1 to 1.2 µg/m^3. According to ECHA's Guidance on information requirements, it is not necessary to submit a confirmatory method on air if acceptable confirmatory methods have been submitted for either soil or water. As an acceptable confirmatory method has been submitted for both soil and water, the confirmatory method for air (Tribolet 2001) is considered sufficient to describe the method on air and no data gap is identified.
Due to the vapour pressure of fludioxonil and the intended use of the biocidal product it is not likely that fludioxonil will become airborne. The adequacy of LOQ is not evaluated as there is no limit in air on work places for fludioxonil and as exposure during inhalation is very limited.

Method on water

Formic acid is added to an aliquot of water and shaken. The sample is cleaned up using a Waters Oasis™ HLB solid phase extraction cartridge (60 mg, 3 mL size) using methanol and water as the eluate. Determination is by HPLC using a ACE 5 µm C183.0 mm x 50 mm column with acetonitrile/0.2% acetic acid in water mobile phase (gradient). Detection is performed by mass spectrometer (API, negative mode) monitoring the following transitions:

Fludioxonil: 246.9 - 179.9 (primary), 246.9 - 125.9 (confirmatory). CGA192155: 201.0 - 90.9 (primary), 201.0 - 156.9 (confirmatory). CGA339833: 311.1 - 267.0 (primary), 311.1 - 65.8 (confirmatory).

The method has been validated and audited as a GLP study (Robinson, 2007 and Nagra, 2007) for fludioxonil and the metabolites CGA192155 and CGA339833 in ground water, drinking water and river water. No interferences were observed. The detector response is linear for seven reference standards within the concentration range from 0.1 to 50 µg/mL. Confirmation simulteaneously to the primary detection of fludioxonil has been performed by using an additional transition for the LC-MS/MS detection.
LOQ for both the primary and confirmatory method is 0.05 µg/L.
LOQ for surface/river water is below the PNECwater = 0.0019 mg/L = 1.9 µg/L and LOQ for drinking water is below the limit of ≤ 0,1 µg/L according to the Drinking Water Directive (DWD).The method is therefore regarded as acceptable by CA DK.

Method on body fluids and tissues
Fludioxonil is not classified as toxic or highly toxic. Therefore, methods for the determination of residues in animal and human body fluids and tissues are not required.

Method on food/feed of plant or animal origin
For the specified uses under PT7, PT9 and PT10, fludioxonil and the formulated product Sporgard WB are not used for the treatment of food or feedingstuffs, or for the treatment of surfaces coming into contact with food or feeding stuffs. Therefore, methods for the determination of residues in food and feedingstuffs are not required.

2 EFFECTS AGAINST TARGET ORGANISMS

2.1 FUNCTION AND FIELD OF USE ENVISAGED

Fungicide for material preservation in PT 7, 9 and 10.

2.2 INTENDED USES

Summary table of intended use(s)	
Product Type	Fludioxonil is intended for use as a biocide active substance within the following product type (PT) areas: Main Group 2: Preservatives PT 7 Film preservatives For PT 7 uses, fludioxonil is formulated as the preservative product Sporgard WB which is added to paints, silicon coatings, mineral sealants and grouts. Other preservative products containing fludioxonil may be used in silicon sealants and grout. PT 9 Fibre, leather, rubber and polymerised material preservatives For PT 9 uses, fludioxonil is formulated as the preservative product Sporgard WB which is added to paper which is used for the production of wall linings. PT 10 Masonry preservatives For PT 10 uses, fludioxonil is formulated as the preservative product Sporgard WB which is added to building materials such as gypsum boards The use of fludioxonil is not intended to protect against food-borne or pathogenic organisms and end use items treated with fludioxonil are not intended for use in food or feed contact areas.
Product description	Fludioxonil is a fungicide that is used in the material preservative product Sporgard WB. Please find product description above.
Target organisms (including development stage)	The fungi usually associated with generation of odours, staining and, more generally, with bio-

<table>
<tr><th colspan="2">Summary table of intended use(s)</th></tr>
<tr><td></td><td>deterioration are part of the division Ascomycota which might belong to different classes e.g.:
<table>
<tr><td>Division</td><td>Class</td><td>Species</td></tr>
<tr><td rowspan="6">Ascomycota</td><td rowspan="3">Sordariomycetes</td><td>Stachybotrys chartarum</td></tr>
<tr><td>Chaetomium globosum</td></tr>
<tr><td>Gliocladium virens</td></tr>
<tr><td>Eurotiomycetes</td><td>Aspergillus niger</td></tr>
<tr><td rowspan="3">Dothideomycetes</td><td>Alternaria alternata</td></tr>
<tr><td>Curvularia lunata</td></tr>
<tr><td>Aureobasidium pullulans</td></tr>
</table></td></tr>
<tr><td>Description of use(s)</td><td>Fludioxonil is not intended to be used as a stand-alone substance, it is intended to be used in combination with other fungicides e.g. with the existing active substance Thiabendazole and/or the new active substance Azoxystrobin to preserve treated materials. Fludioxonil is used in biocidal preservative products which are applied to, or incorporated into various end-applications covering paper, wall boards, masonry and coating/sealing products. Biocidal products containing inter alia the active substance Fludioxonil are intended to inhibit the growth of many fungi associated with odors, staining and, in general, bio-deterioration.</td></tr>
<tr><td>Mode of action</td><td>Fludioxonil belongs to the phenylpyrrole class of fungicides. Fludioxonil is a fungicide that works by inhibiting the osmotic signal pathway which results in the inhibition of spore germination and prevention of mycelia growth. The mode of action of fludioxonil is by inhibition of a mitogen-activated protein (MAP) kinase in signal transduction of osmo-regulation (glycerol synthesis). Fludioxonil acts immediately on the target mode of action and there is no time delay for efficacy.</td></tr>
<tr><td>Objects to be protected</td><td>Materials within PT 7, 9 and 10</td></tr>
<tr><td>Concentration of product in the in-use formulation/product</td><td>
<table>
<tr><td>Biocidal product</td><td>Field of use envisaged</td><td>Concentration of Sporgard WB in end-use material</td></tr>
<tr><td colspan="3">PT 7 Film preservative</td></tr>
</table></td></tr>
</table>

Summary table of intended use(s)

	Sporgard WB	Paints, silicon coatings (aqueous emulsions) Indoor use	0.15-1.6%
		Mineral sealants and grouts Indoor use	0.08-1.6%
	PT 9.02 – Paper preservative		
	Sporgard WB	Paper (drywall lining) Indoor use	0.25-0.5% (dry paper)
	PT 10 Masonry preservative		
	Sporgard WB	Drywall gypsum powder Indoor use	0.05-1.6%
Concentration of active substance in the in-use formulation/product	**Biocidal product**	**Field of use envisaged**	**Concentration of fludioxonil in end-use material**
	PT 7 Film preservative		
	Sporgard WB	Paints, silicon coatings (aqueous emulsions) Indoor use	max. 0.032% min. 0.003%
		Mineral sealants and grouts Indoor use	max. 0.032% min. 0.002%
	PT 9.02 – Paper preservative		
	Sporgard WB	Paper (drywall lining) Indoor use	max. 0.010% min. 0.005%
	PT 10 Masonry preservative		
	Sporgard WB	Drywall gypsum powder Indoor use	max. 0.032% min. 0.001%
Application rate(s)	Fludioxonil in combination with other fungicides are added during material production; the preservatives prevents bio-deterioration during service life.		
Frequency of application	Fludioxonil in combination with other fungicides are added during material production; the preservatives prevents bio-deterioration during service life.		
Season/period for use (where relevant)	Not relevant.		

Summary table of intended use(s)	
Field of use (indoors/outdoors)	Fludioxonil is a fungicide that is used in the material preservative biocidal product Sporgard WB. Sporgard WB can be applied to, or impregnated into materials such as: water-based paints and coatings.. Furthermore in mineral sealants and grouts, paper used in drywall production and gypsum powder used in drywall construction. These treated materials are used indoors
Category(ies) of user(s)	The end-use treated items may be used by professional workers and by the general public (non-professional), depending on the individual item.
Instruction for use	Fludioxonil in combination with other fungicides are added during material production. The manufacture of fludioxonil and formulation of the biocidal product Sporgard WB is conducted industrially outside the EU. Incorporation of Sporgard WB into the end-use items and materials is conducted industrially within the EU.

2.3 SUMMARY ON EFFICACY

2.3.1 Efficacy

Experimental data on the efficacy of the active substance against target organism(s)						
Function and field of use envisaged	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
Fungicide for material preservation in PT 7, 9 and 10	FDL, [redacted] w/w Fludioxonil	*Alternaria alternata, Aspergillus niger, Aureobasidium pullulans, Chartomium globosum, Fusarium solani, Gliocladium virens, Penicillium funicolosum, Stachybotrys chartarum, Paecilomyces funiculosum*	Test was performed according to internal methods of the test laboratory which were attached to the original report M 2 02-00012-12. Agar plate test. Evaluation was carried out by measuring the	The concentration of test substance fludioxonil at which fungi growth can no longer be detected was determined and is stated as the minimum inhibitory concentration (MIC). The MIC values are given in ppm. The following concentrations were tested: 0, 1, 5, 10, 20, 30, 40, 50, 75, 100, 250, 500 ppm, respectively.	The MIC (minimum inhibitory concentration) values of fludioxonil against *Alternaria alternata* and *Stachybotrys chartarum* were in the range between 1 ppm and 5 ppm. For all other tested *Ascomycota* and *Deuteromycota*, fludioxonil showed no efficacy, MIC > 500ppm.	Gerharz, T. (2014) (IUCLID 6.6-01)

			radial growth of the fungi on the control plates without fungicide as well as on fungicide amended medium. The results were expressed as % activity relative to the check.			
Fungicide for material preservation in PT 7, 9 and 10	Fludioxonil WP [redacted] fludioxonil and Fludioxonil [redacted] fludioxonil	*Alternaria alternata, Alternaria tenuissima, Aspergillus niger, Aspergillus versicolor, Aureaobasidium pullulans, Chaetomium globosum, Cladosporium cladosporioides, Coniophora puteana, Gloephyllium trabeum, Oligoportus placenta, Penicillium citrium, Penicillium funiculosum, Penicillium pinophilum, Stachybotrys chatarum, Sydowia pythiophila, Trametes versicolor, Trichoderma viride*	Activity of Fludioxonil WP studied on the basis of EC 50 (mg ai/l) and EC 95 (mg ai/l). Furthermore the activity was compared between Fludioxonil WP and Fludioxonil SC	AE sporulation medium (AE-agar) was cooled down to 55°C before fludioxonil was added. The AE-agar with fludioxonil was poured out in plastic petri dishes. After one day one mycelial plug per test petri dish was taken with a cork borer from the stem cultures and transferred upside down onto the solid surface of the fungicede conaining agar. The following concentrations were tested: 0, 1, 10, 100, 1000, 5000 ppm, respectively. The assays were evaluated when approx. 2/3 of the surface of the check dishes was covered with mycelium. The evaluation was carried out by measuring the radial growth of the fungi on control plates without fungiced as well as on fungicide amended medium. The results are expressed as % activity relative to the check.	Fludioxonil WP 50 provides partial activity against a broad range of fungi but it has some gaps such as *Aureaobasidium pululans*,*Chaetomium globosum* and *Trichoderma viride*. It provides specific activities against some *Penicillium* spp., *Alternaria* spp. and some wood decaying fungi, such as *Conophora puteana*, *Gloeophyllum trabeum* and *Sydowia pythiophila*". EC50 values are less than 1 mg/L for the majority of organisms tested, except for *A. niger*, *A. pululans*, *C. globosum* and *T. viride*. EC50 are less than 0.1 mg/L for *A. alternata*, *P. pinophillum* and *S. pythiophila.* No significant	Knauf-Beiter, G.; Gerber, T.; Theiler, M. (2005) (IUCLID 6.6-02)

					differences of the activity were found between fludioxonil in the two formulations.	

2.3.2 Mode of action

Fludioxonil belongs to the phenylpyrrole class of fungicides.The mode of action of fludioxonil is by inhibition of a mitogen-activated protein (MAP) kinase in signal transduction of osmo-regulation (glycerol synthesis). Fludioxonil is a fungicide that works by inhibiting the osmotic signal pathway which results in the inhibition of spore germination and prevention of mycelia growth. Fludioxonil acts immediately on the target mode of action and there is no time delay for efficacy.

2.3.3 Resistance

Fludioxonil has a single site mode of action. Fungicides with a single site mode of action are more prone to the development of resistance because any change(s) that might occur in the fungus to alter that single site could render the fungus resistant to the fungicide. The potential for resistance development therefore exists, but is restricted by the manner in which fludioxonil is used in the biocidal product.

Typical management strategies for fungicide resistance include; not using sub-lethal application rates that may select for fungicide resistance and applying mixtures of two or more fungicides that have different modes of action. Fludioxonil is intended for use mainly in combination with other fungicides, like the product Sporgard WB which contains a mixture of fungicides that present different modes of action. The action of Sporgard WB will therefore be multi-site and the possibility of resistance development is considerably reduced.

2.4 CONCLUSION ON EFFICACY

Fludioxonil is a fungicide intended for use as a preservative within the product type PT 7, 9 and 10. The presence of fludioxonil in treated items inhibits the growth of some specific fungi associated with odours, staining and general bio-deterioration. Efficacy data of fludioxonil shows a specific innate activity against the target fungi *Alternaria alternata* and *Stachybotrys chartarum*. *Stachybotrys chararum* is a common fungal species causing black mold staining on damp indoor surfaces, whilst *Alternaria alternata* is another black pigmented mold that can be isolated from building materials. Furthermore selected efficacy data from the Syngenta report (Knauf-Beiter, G.; Gerber, T.; Theiler, M. (2005)) shows that fludioxonil provides inate activities against some *Penicillium* spp., *Alternaria spp*. and some wood decaying fungi, such as *Conophora puteana*, *Gloeophyllum trabeum* and *Sydowia pythiophila*". Whereas no activity was found against *Aureaobasidium pululans*,*Chaetomium globosum* and *Trichoderma viride*.

Fludioxonil shows an adequate innate fungicidal activity for use as a preservative within the product type PT 7, 9 and 10. However, it is a prerequisite that fludioxonil is used in combination with other fungicides.

3 ASSESSMENT OF EFFECTS ON HUMAN HEALTH

The batches used in the key toxicological studies covers the current technical specification and therefore the toxicological assessment of fludioxonil. Please refer to Annex VI in this CAR to document "Evaluation of the representativeness of the technical specification of fludioxonil in the batches used in the toxicological studies" prepared for the Ad hoc follow up WG_IV 2016 for fludioxonil-tox batches.

3.1 TOXICOKINETICS

Method **Guideline, GLP status,** **Reliability**	**Species,** **Strain,** **Sex,** **No/Group**	**Test substance,** **Dose levels** **Duration of exposure**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 417 (1984); fulfilled together with the additional studies listed below. GLP 1	Rat (Tif: RAIf (SPF) m/f	Fludioxonil (Non-radiolabelled: > [redacted]; Radiolabelled: [redacted]) gavage Single low dose (0.5 mg/kg bw); Group B, E & F Single high dose (100 mg/kg bw; bile duct cannulated females and non bile duct cannulated): Group G2 & D Repeated low dose (0.5 mg/kg bw); Group C	None	[redacted], 1990 (IUCLID 8.8.1-01)
The study was performed to FIFRA 85-1. GLP	-	Samples of urine, bile and faeces were taken from the following groups of animals in the kinetics study ([redacted], 1990)	-	[redacted] 1992 (IUCLID 8.8.1-02)

Method **Guideline, GLP status,** **Reliability**	**Species,** **Strain,** **Sex,** **No/Group**	**Test substance,** **Dose levels** **Duration of exposure**	**Remarks** *(e.g. major deviations)*	**Reference**
1		5/sex (Groups B, C, D); 5 females (Group G2)		
OECD guideline no. 417 GLP 1	Rat (Tif:RAIf (SPF) m/f	Fludioxonil (Non-radiolabelled: > [redacted]; Radiolabelled: [redacted]) Single low dose (0.5 mg/kg bw.); Group E1, E3, F1 & F3 Single high dose (100 mg/kg bw.); Group E2, E4, F2 & F4 3/sex/group	None	[redacted]., 1995 (IUCLID 8.8.1-03)
None (investigate study) Sub-groups of animals from the 2-year chronic toxicity study in rat.	Rat (Crl:CD(SD)BR) m	Fludioxonil (radiochemical purity [redacted] unlabelled fludioxonil [redacted] purity) Two dosed males and 1 control male per time point.	-	[redacted]. 1994 (IUCLID 8.8.1-04)

3.1.1 Short summary of the toxicokinetic information

Absorption, distribution, excretion and metabolism in mammals (ADME)
The absorption, distribution and metabolism of fludioxonil were investigated in the rat using radiolabelled test material in four studies ([redacted]). Evaluated together the studies from [redacted] (1995) fulfill the requirements of 87/302/EEC B.36 and OECD 417 (1984).The results of these studies is described below:

Fludioxonil was rapidly absorbed following oral administration to the rat; maximum blood levels were attained within 30 minutes. Figures for the excretion of radioactivity in bile duct cannulated rats indicate that at least 77.5% of the administered dose was absorbed from the gastrointestinal tract into the systemic circulation within 48 hours. The actual amount of excreted radioactivity is likely to be greater than this amount due to the loss of one bile sample from one animal. It is also notable that the total amount of radioactivity recovered from excreta (urine + faeces + bile) in this study is relatively low (91.8% of the administered radioactivity), indicating a level of residual radioactivity in the carcass and/or gastrointestinal tract of approximately 8%. The incomplete excretion of radioactivity by the bile duct-cannulated rats of Group G from 0-48 hours following dosing is consistent with the pattern seen for Groups B, C and D, in which excretion during the first 24 hours accounted for approximately 75-90% of the administered dose and excretion within 7 days accounted for 94-97% of the administered dose. It is also known that excretion may be slower in bile duct-cannulated rats. It can therefore be concluded that the total level of radioactivity absorbed by the bile duct cannulated rats is likely to exceed 80% of the administered dose.
Fludioxonil was excreted in urine (13-20%) and to a greater extent (78-83%) in faeces; the majority of the faecal radioactivity (68% of the administered dose) was found to be of biliary origin and there is evidence for a degree of enterohepatic recirculation. Residues were low in all tissues, but were comparatively high in the liver and kidney, reflecting biliary and urinary excretion; there is no evidence for accumulation. Tissue residues accounted for 0.06% of the administered low dose and 0.17 % of administered high dose after 7 days. Absorbed fludioxonil was completely metabolised, with 20 metabolites detected in urine. Unchanged fludioxonil was the only identified component in faeces (Bissig, 1990) and the unchanged parent compound was not found in urine. The metabolite pattern was complex but appeared to be independent of sex, dose level, and pre-treatment.

Following a single low or high oral dose of fludioxonil to rats, absorption was rapid, as was the clearance of radioactivity from blood. AUC values indicate a slightly lower level of absorption in both sexes at the high dose level and also indicate slightly lower systemic exposure in females at both dose levels.
Tissue concentrations of radioactivity declined rapidly: no accumulation or retention of fludioxonil or its metabolites is predicted ([redacted], 1995).
Fludioxonil was extensively metabolised. In the urine, five different metabolites were identified of which four were identical to those identified in the bile (G2 group; bile cannulated 100 mg/kg bw). Three metabolites (urine and bile) representing about 57%, 4% and 2% of the administered dose and, together with unchanged fludioxonil, represent a cumulative total of approximately 75% of an oral dose

Metabolism involved oxidation of the pyrrole ring, hydroxylation of the phenyl ring and conjugation with glucuronic acid and sulphate. The major metabolites were identified as the glucuronide and sulphate conjugates of the hydroxylated metabolite SYN 51877 ([redacted] 1992).
Urine from animals exposed to high dietary doses (1000 and 3000 ppm) for a prolonged period showed a blue colouration. This colouration was due to a metabolite of fludioxonil, which was identified as a dimer formed by metabolic oxidation of the pyrrole moiety followed by autoxidative dimerisation. The coloured dimer accounted for about 1-2 % of the daily intake of 3000 ppm fludioxonil in male rats

([redacted], 1994). The formation of this metabolite accounts for the coloration of excreta and various tissues in the standard toxicity studies.

A default value of 100 % is used for inhalatory absorption (no study was performed).

Dermal absorption

For the evaluation of the dermal absorption of the representative product Sporgard WB five studies have been submitted of which only four of these will be evaluated and presented in this CAR. The fifth was evaluated by EFSA for the PPP use of fludioxonil and judged not reliable due to several short-comings in the study, which will be summarized shortly below under the specific study (Hassler, 1999).

None of the studies are performed on Sporgard WB but on two other formulations, **Switch 62.5 WG** alias **Fludioxonil/cyprodinil 62.5 WG and** ([redacted]) and Fludioxonil 230 g/l SC formulation ([redacted]); both containing fludioxonil.

The five studies submitted are the following:

***In vitro* studies:**
Davies D J (2005); Fludioxonil/cyprodinil 62.5 WG ([redacted]): In vitro dermal absorption of fludioxonil through rat epidermis

Davies D J (2005): Fludioxonil/cyprodinil 62.5 WG ([redacted]): In vitro of fludioxonil through human epidermis

Davies D J. 2005. Fludioxonil 230g/l SC formulation ([redacted]): *In vitro* dermal absorption of fludioxonil through human epidermis.

Hassler S. 1999. The in vitro percutaneous absorption of [Phenyl-U-14C] CGA 173506 formulated as SWITCH 62.5 WG ([redacted]) through rat and human epidermis.

***In vivo* rat study**
[redacted]., 1999. Dermal absorption of [Phenyl-U-^{14}C] CGA 173506 formulated as SWITCH® 62.5 WG ([redacted]) in the rat.

The *in vitro* study performed by Hassler, 1999 had several short comings, see below, is not considered reliable and can therefore not be used as a key study and has not been tabulated in the summary table of *in vitro* studies.

"In the rat skin the residues in the skin after 48 hours were 3.5 % at the low dose and 16.4 % at the high dose. In the human skin the residues after 48 hours were 1.8% at the low dose and 79.2% at the high dose. The results in human skin at the high dose do not seem reliable when compared with the other results and the results from the skin rinsing etc. from the other samples. It looks that the rinsing procedure has not been satisfactorily performed in the high dose.

The study is performed according to a draft guideline from 1996 and is mainly performed to generate good flux data. According to the study report the amount of radioactivity could not be reliably assigned

to the compartments cell wash, epidermis, and skin rinse due to the small size and fragility of the epidermal membrane.

The dermal absorption values set by EFSA are based on the three studies performed on Switch 62.5 WG alias Fludioxonil/cyprodinil 62.5 WG (Davies 2005; *In vitro* rat and human epidermal membranes and [redacted] 1999*: in vivo* rat study)

Summary table of *in vitro* studies on dermal absorption					
Method, Guideline, GLP status, Reliability	**Test substance, Doses**	**Relevant information about the study**	**Absorption data for each compartment and final dermal absorption value (%)**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 428 GLP *In vitro* rat epidermis	Fludioxonil/cyprodinil 62.5 WG ([redacted]) 6 and 24 hr exposure Concentrate (249 g fludiozonil/kg) 1/667 w/v dilution (0.39 g fludioxonil /L) Application rate 10 mg/cm^2 10 µL/cm^2 Area dose 2490 µg/cm^2 3.94 µg/cm^2	Male rats (skin from dorsal and flank regions)	**Dilution** (0.039% fludioxonil) Receptor fluid: 17.6% Epidermis: 12.8 Total (6 hr): 30.4% **Concentrate** (25% fludioxonil) Receptor fluid: 1.26% Epidermis: 0.05 Total (24 hr): 1.28%	-	Davies D J, 2005 (IUCLID 8.8.2-04)

OECD 428 GLP *In vitro* human epidermis	Fludioxonil/cyprodinil 62.5 WG ([redacted]) 6 and 24 hr exposure Concentrate (249 g fludiozonil/kg) 1/667 w/v dilution (0.39 g fludioxonil /L) Application rate 10 mg/cm^2 10 µL/cm^2 Area dose 2490 µg/cm^2 3.94 µg/cm^2	Skin samples from humans obtained from surgery or *post mortem*	**Dilution** (0.039% fludioxonil) Receptor fluid: 2.63% Epidermis+stratum corneum: 1.38 Total (24 hr): 4% **Concentrate** (25% fludioxonil) Receptor fluid: 0.01% Epidermis+stratum corneum: 0.1 Total (24 hr): 0.11%	Sex and part of skin not specified.	Davies D J, 2005 (IUCLID 8.8.2-05)

OECD 428 GLP *In vitro* human epidermis (key study)	Fludioxonil 230 g/l SC formulation ([redacted]) 6 and 24 hr exposure Concentrate (233.3 g fludiozonil/kg) 1/380 w/v dilution (0.47 g fludioxonil /L) Application rate 10 µL/cm^2 Area dose 2 µg/cm^2 4.67 µg/cm^2	Skin samples from humans; not specified	**Dilution** (0.05% fludioxonil) Receptor fluid: 0.55% Epidermis+stratum corneum (all tape strips) 1.61 Total (6 hr)**: 2.74 (mean 2.2+ 1 SD 0.54) Total (24 hr)*: 3.04 **Concentrate** (23.3% fludioxonil) Receptor fluid: 0.02% Epidermis+stratum corneum (all tape strips) 0.12 Total (6 hr): 0.2% (mean 0.15+ 1 SD 0.05) ** Total (24 hr): 0.87%	Part of skin not specified.	Davies D J, 2005 (IUCLID 8.8.2-03)

*Specific figures not tabulated in this table
** exposure duration of 6 hours (no sampling continued), the whole skin has to be included for the derivation according to EFSA GD ("If sampling does not continue for an adequate period, include all material in the skin sample/at the application site or, if possible, extrapolate to an adequate time point").

The ***in vitro*** **rat skin study** with Fludioxonil/cyprodinil 62.5 WG ([redacted]) was performed in accordance with the OECD Guideline 428 for *in-vitro* percutaneous absorption. The distribution of fludioxonil within the test system (skin wash, donor chamber, and epidermis) and an absorption profile (µg/cm^2/hr) over a full 24 hour exposure period were determined.

The dermal penetration *in vitro* was assessed by single topical application of the formulation concentrate (249 g fludioxonil/kg ~25% fludioxonil) and about 0.39 g fludioxonil/L ~0.039% fludioxonil (applied as dilution). Groups of cells, for each dose preparation, were assigned to each exposure periods, 6 or 24 hours. No individual tape stripping was performed. The epidermis was carefully peeled from the dermis.

Dilution (0.039% fludioxonil)

The mean total recovery measured (92.9% and 97.8%) in diffusion cells equipped with rat skin at the low dose fulfilled the OECD quality criteria (100 % ± 10 %). The individual values ranged between 89.9% and 102%. The major amount of test substance was found by skin washing while 12.8% and 10.8% of the test substance was associated with the skin membrane at 6 and 24 hours exposure, respectively, and about 17.6% and 19.4% were recovered from the receptor fluid. A larger range of absorption were observed in the first hours after application indicated by the cumulative amount recovered and a higher adsorption rate.

The amount of test substance recovered in the epidermis was lower after 24 hours than after 6 hours (not significant) indicating that the amount in the epidermis was available for absorption. The total amount of absorbed substance includes the amount of substance recovered in the epidermis membrane (in compliance with FLOW CHART 4a in EFSA Guidance on dermal absorption, 2012) giving a total dermal penetration of approximately 30.4 % (6 hr. exposure) for fludioxonil through rat skin.

Concentrate (25% fludioxonil)

The mean total recovery measured (92.6% and 96.1%) in diffusion cells equipped with rat skin at the high dose fulfilled the OECD quality criteria (100 % ± 10 %). The individual values ranged between 81.7% and 103% indicating that only one cell exceeded the OECD quality criteria (81.7 %). As the results of this cell, however, fitted well into the overall range of measurements for recovery as well as kinetics, the cell was not discarded.

The major amount of test substance was found by skin washing. About 0.16 – 1.23% of the test substance was associated with the skin membrane, while about 0.01 – 0.05% were recovered from the receptor fluid. The total amount of absorbed substance included the amount of substance measured in the epidermis membrane (according to Flow Chart 4a in EFSA Guidance on dermal absorption, 2012) giving a total penetration of **maximum 1.28% for fludioxonil formulated as a concentrate (taken from the 24 hr exposure).**

Kinetic parameters:

For the concentrate, fludioxonil absorption was linear over the entire 24 hour exposure period. Between 0-24 hours, the rate of absorption was 0.05 µg/cm^2/hr. For the 1/667 w/v aqueous dilution, fludioxonil absorption was fastest (0.15 µg/cm^2/hr) between 0-1 hours. Between 1-24 hours the absorption rate slowed down to 0.03 µg/cm^2/hr.

Except for the first hour after application of the test compound to the rat skin, the high dose penetrated the membrane with a higher rate than the low dose. However, in comparison to the 640-fold difference in high and low dose concentrations, the difference in penetration rates through rat skin were only 1.6-fold. This indicated saturation of the skin after application of the high dose.

Conclusion:

The study is considered acceptable for the evaluation of the skin absorption of fludioxonil *in vitro.*

The studies showed that fludioxonil in a concentrate formulation was absorbed slowly through rat epidermis (0.05%/24 hr); while fludioxonil formulated in a dilution similar to a typical 1/667 w/v aqueous dilution was absorbed moderately (19.4%/24 hr).

For both the concentrate and the dilution the majority of the test material was recovered from the surface of the skin by mild skin wash.

In this *in vitro* rat skin study a total dermal absorption of maximum 30.4% (6 hr) was observed for fludioxonil formulated as a 1/667 w/v aqueous dilution. Dermal absorption of maximum 1.28% (24 hr) was observed for fludioxonil in a concentrate formulation.

The ***in vitro*** **human skin study** with Fludioxonil/cyprodinil 62.5 WG ([redacted]) was performed in accordance with the OECD Guideline 428 for *in-vitro* percutaneous absorption. The distribution of fludioxonil within the test system (skin wash, donor chamber, stratum corneum and epidermis) and an absorption profile (µg/cm^2/hr) over a full 24 hour exposure period were determined.

The dermal penetration *in vitro* was assessed by single topical application of the formulation concentrate (249 g fludioxonil/kg ~25% fludioxonil) and about 0.39 g fludioxonil/L ~0.039% fludioxonil (applied as dilution). Groups of cells, for each dose preparation, were assigned to each exposure periods, 6 or 24 hours. Stratum corneum was removed by repeated application of adhesive tape to a maximum of 5 strips, these were pooled.

Dilution (0.039% fludioxonil)
The mean total recovery measured (93.0 and 94.7%) in diffusion cells equipped with human skin at the low dose fulfilled the OECD quality criteria (100 % ± 10 %). The individual values ranged between 90.2% and 97.8%.

The major amount of test substance was found by skin washing (about 90% at both 6 and 24 hours exposure). About 1.5% of the test substance was associated with the skin membrane (stratum corneum and remaining epidermis), while 1 and 2.6% was recovered from the receptor fluid at 6 and 24 hours exposure, respectively. The amount of test substance recovered in the epidermis was lower after 24 hours than after 6 hours indicating that the amount in the epidermis was available for absorption. Since the stratum corneum strips were pooled the first 1-2 strips cannot be excluded from the dermal absorption (in compliance with EFSA Guidance on dermal absorption, 2012). Therefore, the total amount of absorbed substance includes the amount of substance recovered in the epidermal membrane and stratum corneum giving a total penetration of approximately 2.58% and 4.01% at 6 and 24 hours exposure, respectively, for fludioxonil through human skin *in vitro*.

Concentrate (25% fludioxonil)
The mean total recovery (93.0 and 94.5%) measured in diffusion cells equipped with human skin at the high dose exposed 6 and 24 hours respectively fulfilled the OECD quality criteria (100 % ± 10 %). The individual values ranged between 83.3% and 102%. Two individual cells did not fulfil the OECD quality criteria as they had a recovery below 90%. However, as the results of these cells fitted well into the overall range of measurements for recovery as well as kinetics, the cells were not discarded.

The major amount of test substance was recovered by skin washing (mean between 91.2 and 93.9% at 6 and 24 hours, respectively). About 0.1% of the test substance was associated with the skin membrane (stratum corneum and remaining epidermis), while less than 0.01% were recovered from the receptor fluid. For *in vitro* studies, the total amount of absorbed substance included the amount of substance measured in the epidermis membrane giving a total penetration of about 0.11% (24 hr) for fludioxonil

formulated as a concentrate through human skin *in vitro*. The maximum dermal absorption was 0.12% from the 6 hr exposure group however the values is considered equal due the neglibel difference.

Kinetic parameters
For the concentrate, fludioxonil absorption was linear over the entire 24 hour exposure period. Between 0-24 hours, the rate of absorption was less than 0.01 µg/cm^2/hr. For the 1/667 w/v aqueous dilution, fludioxonil absorption was fastest (0.01 µg/cm^2/hr) between 0-2 hours. Between 2-24 hours the absorption rate slowed down to 0.004 µg/cm^2/hr.

Except for the first two hours after application of the test compound to the human skin, the high dose penetrated the membrane with a higher rate than the low dose. However, in comparison to the 640-fold difference in high and low dose concentrations, the difference in penetration rates through human skin were only 2.5-fold. This indicated saturation of the skin after application of the high dose.

Conclusion
The study was conducted according to GLP and OECD guidelines. It is acceptable for the evaluation of the skin absorption of fludioxonil *in vitro.*

The mean total recovery ranged between 93 % and 94.7 % of the applied dose of fludioxonil. The studies showed that fludioxonil in a concentrate formulation was absorbed very slowly through human epidermis (0.01%/24 hr); while fludioxonil formulated in a dilution similar to a typical 1/667 w/v aqueous dilution was absorbed slowly (2.63%/24 hr).

For both the concentrate and the dilution the majority of the test material (about 90-94%) was recovered from the surface of the skin by mild skin wash. Another part of the test substance was recovered in the stratum corneum and remaining epidermis. As this study did not demonstrate whether the amount of substance found in the skin at 24 hours could be absorbed at a later stage or not the amount of substance retained in the stratum corneum and remaining epidermis should be included as absorbed.

In this study a total dermal absorption of maximum 4.01% was observed for fludioxonil formulated as a 1/667 w/v aqueous dilution. Dermal absorption of about 0.11% was observed for fludioxonil in a concentrate formulation through human skin.

The ***in vitro* human skin study** with Fludioxonil 230 g/l SC formulation ([redacted]) was performed in accordance with the OECD Guideline 428 for *in-vitro* percutaneous absorption. The distribution of fludioxonil within the test system (skin wash, donor chamber, stratum corneum and epidermis) and an absorption profile (µg/cm^2/hr) over a full 24 hour exposure period were determined.

The dermal penetration *in vitro* was assessed by single topical application of the formulation concentrate (230 g fludioxonil/kg ~23.3% (w/v) fludioxonil) and about 0.47 g fludioxonil/L ~0.05% fludioxonil (applied as dilution). Groups of cells, for each dose preparation, were assigned to each exposure periods, 6 or 24 hours. Stratum corneum was removed by repeated application of adhesive tape to a maximum of 5 strips analysed individually.

Some recovery values were below 95% (90.0-93.9%) in the low dose after both 6 hours (2/6 wells) and

24 hours (3/6 wells). It seems most likely that the losses were in the non-absorbed dose when low and high recovery animals/wells are compared indicated by the values from the skin wash, stratum corneum and absorbed dose.

Overall the recoveries are considered acceptable and fulfils the OECD quality criteria (100 % ± 10 %).

The majority (90-101%) of the test substance was found in skin wash after both low and high dose. In the low dose group (24 hours) about 2% was found in the skin (epidermis and stratum corneum), while in the high dose it amounted to 1% also after 24 hours. After 8 hours exposure the figures were 1.61% and 0.12% in the skin (epidermis and stratum corneum) in the low and high dose groups, respectively. The amount recovered from the receptor fluid at 6 and 24 hours were 0.55% and 1.78%, respectively in the low dose and 0.02% and 0.02 % respectively in the high dose group.

Kinetic parameters

For the low dose the rate of absorption was fast 0.011 µg/cm^2/hr between 0-2h. For the 1/667 w/v aqueous dilution, fludioxonil absorption was fastest (0.01 µg/cm^2/hr) between 0-2 hr. Between 2-24 hr the absorption rate slowed down to 0.003 µg/cm^2/hr. Between 2-24 hr the mean absorption rate was 0.003 µg/cm^2/hr. The absorption rate for the high dose were <0.02 µg/cm^2/hr during 0-24 hr; all values were either close to or below LOQ of 0.56 ug/cm^2.

Conclusion

The study was conducted according to GLP and OECD guidelines. It is acceptable for the evaluation of the skin absorption of fludioxonil *in vitro* in human skin membranes.

In compliance with EFSA Guidance on dermal absorption (2012) flow chart 4a and related text* the total dermal absorption is calculated from the absorbed dose (receptor fluid), reservoir in skin and stratum corneum (including all tape strips) from the 6 hours exposure point which should represent a typical working day. All tapes strips were included as absorbed since there was no sampling after the 6 hours exposure period and an additional SD was added to the mean due to SD>25% .

Therefore, the total dermal absorption after 6 hours exposure would be 2.7 % for the low dose (0.05% fludioxonil) and 0.2% for the concentrate (23.3% fludioxonil).
* If sampling does not continue for an adequate period, include all material in the skin sample/at the application site or, if possible, extrapolate to an adequate time point").

Summary table of animal studies on dermal absorption						
Method, Guideline GLP status, Reliability	**Species, Strain, Sex, No/group**	**Concentration of test substance/Label Duration of exposure**	**Signs of toxicity**	**Absorption data for each compartment and final dermal absorption value**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 427 GLP 1 *In vivo* rat study	Male rat (SPF) 12/dose group	Dilutions of formulated Fludioxonil/cyprodinil 62.5 WG ([redacted])* Applied dose Low (0.048% fludioxonil): 4.5 µg/cm^2 High (6.7% fludioxonil): 558 µg/cm^2 6 hr exposure followed by wash of treated skin area (sampling time 6 hr, 24 hr and 48 hr). No tape stripping.	Slight weight loss in high dose animals	Dermal absorption (skin residues + systemic absorption) Low dose (0.048% fludioxonil): ~13% High dose (6.7% fludioxonil): ~3.3%	-	[redacted] 1999 (IUCLID 8.8.2-02)

** Switch 62.5 WG alias Fludioxonil/Cyprodinil 62.5 WG ([redacted]) contains both fludioxonil and cyprodinil at nominal concentrations of 250 g/kg and 375 g/kg, respectively. 1) High dose: a 1:37 (w/v) aqueous dilution of the formulated test substance a Switch 62.5 WG 2) Low dose (P1): a 1/520 (w/v) aqueous dilution of the formulated test substance a Switch 62.5 WG. This corresponds to a fludioxonil content of 67 g/l ~ 6.7% for high dose and 0.48 g/l ~0.048% for the low dose assuming a density of water of (1000g =1 L).*

The ***in vivo* rat study** with Fludioxonil/cyprodinil 62.5 WG ([redacted]) was performed in line with the OECD Guideline 427. Two groups of each 12 male rats were exposed to a low dose of (0.048% fludioxonil) and high dose (6.7% fludioxonil). The dose groups were further divided into subgroups consisting of 4 animals each – sacrifice groups T1: 6 hours after dose application, T2: 24 hours after dose application, and T3: 48 hours after dose application. Exposure time was 6 hours hereafter the skin wash with a mild soap solution using cotton swaps followed by 48 hours sampling period. No tape stripping were performed.

The majority of the applied test substance was recovered in the skin wash (76.5- 90.5 % of the dose). At both dose levels only a small amount was excreted in urine with 0.15 % at the low dose and < 0.01 % at the high dose after 6 hours of application and 1.01 % at the low dose and 0.08 % at the high dose at 48 hours after start of exposure. The main excretion route was via faeces and most of the applied dose was excreted between 6 and 24 hours after start of exposure but there was still excretion between 24 and 48 hours after start of exposure indicating further absorption of the residues in the skin. As the excretion is not followed for longer than 48 hours and as there is still excretion after 48 hours, the residues in skin shall be included in the dermal absorption value.

The percentage absorption is higher in the low dose than in the high dose. In the low dose the average systemic absorption after 48 hours was 7.4 % and the residues in skin was 5.7%. Therefore the dermal absorption at the low dose was 13.1%. At the high dose the average systemic absorption after 48 hours was 0.6% and the residues in the skin was 2.7%. Therefore the dermal absorption at the high dose was 3.3%.
The corresponding figures after 24 hours are 13.6% for the low dose and 4.6% for the high dose. As the residues in the skin differs somewhat at the different sampling points especially in the high dose it is found acceptable to use the figures for the 48 hours (also in accordance with the EFSA guidance on dermal absorption point 5.8 i which prescribes using data from the terminal sampling time for the *in vivo* rat studies).
The recovery is not so high but considered acceptable.

Conclusion:
Under the condition of this study performed in line with OECD guideline 427 (Skin absorption: *In vivo* Method) with Fludioxonil formulated as Switch 62.5 WG fludioxonil showed limited dermal absorption.
The dermal absorption including all skin residues were 13.1 % for the low dose (0.048% fludioxonil) and 3.3 % for the high dose (6.7% fludioxonil).

At the low dose level, the blood concentrations were below the limit of determination at all time points and at the high dose level, the radioactivity reached a maximum at 0.017 ppm Fludioxonil equivalents after 0.5 hours and decreased thereafter rapidly to or below the limit of determination. The mean penetration rate was calculated to 0.0284 µg/cm^2· h at the low dose level and to 0.0774 µg/cm^2/h at the high dose level. The systemically absorbed dose was rapidly eliminated mainly via faeces.

General note: Even though EFSA guidance on dermal absorption prescribes that the exposure duration should mimic a normal working day (6-10 hr) the dermal absorption after 24 hr has been choosen in most cases to represent worst case and is in line with the EFSA review on fludioxonil (PPP). In one case the dermal absorption value after 6 hr exposure was choosen (in vitro rat epidermal membranes) since this values was a bit higher than after 24 hr, 30.4 % versus 30.2; at this time point the standard deviation of the mean value of the absorbed dose was high (17.6 ± 13.1). It could be argued that the 6 hr exposure time is more realistic however worst case assumption has been taken here to be in consistency with the EFSA conclusion an as proposed by the applicant.

Overall conclusion on dermal absorption based on the studies performed on Fludioxonil/cyprodinil 62.5 WG (Davies, 2005. *In vitro* dermal absorption of fludioxonil through rat epidermis and human epidermis and [redacted], 1999. I*n vivo dermal absorption rat study)*

The dermal absorption percentages based on the two *in vitro* studies are:

Concentrate:
In vitro human absorption (skin plus receptor medium) is 0.12 % and rat *in vitro* absorption is 1.28 %.

Dilution:
In vitro human absorption (skin plus receptor medium) is 4.01 % and rat *in vitro* absorption is 30.4 %.

Overall dermal absorption
Based on *in vivo* and *in vitro* studies the dermal absorption in percentage can be calculated based on the following equation:

Dermal absorption percentage = *in vivo* animal absorption x *in vitro* human absorption/*in vitro* animal absorption.

Based on the *in vivo* dermal absorption data in rat of **Fludioxonil/cyprodinil 62.5** which is 13.1 % of the low and 2.7 % of the high dose the dermal absorption can be calculated to:

Concentrate:
2.7 x 0.12/1.28 % = 0.253 % ~ 0.3 %

Dilution:
13.1 x 4.01/30.4 % = 1.728 % ~ 1.7 %

However the premise for using this equation seems not to be fulfilled, for the concentrate at least, since the area dose (concentration) in the *in vitro* studies differs from the *in vivo* rat study by a factor of 4.5 (558 ug/cm^2 versus 2490 ug/cm^2).

Consideration of the extrapolation from different formulation types:
A comparison of the different formulations with the formulation applied for in this CAR is necessary to justify the extrapolation of the dermal absorption value. None of the studies are performed on Sporgard WB but on two other formulations, **Switch 62.5 WG** alias **Fludioxonil/cyprodinil 62.5 WG and** ([redacted]) and Fludioxonil 230 g/l SC formulation ([redacted]); both containing fludioxonil.
Switch 62.5 WG (a water dispersible granules) and Celest 025 FS (a flowable concentrate) were considered comparable by EFSA and readacross from Switch 62.5 WG to Celest 025 FS were done (after considering the coformulants and the fact that the a.i content in the latter was 10x higher).
According to applicant Sporgard WB is an aqueous dispersion and the type of formulation can be described as a suspension concentrate (SC).

Using the EFSA guidance on dermal absorption (2012) point 6.2 neither of the formulations strictly fulfils the within ±25% w/w difference in coformulants to the reference formulation. However Fludioxonil 230 g/l SC formulation and Sporgard WB are more similar in terms of types of coformulants and the concentrations of these. Furthermore Fludioxonil 230 g/l SC formulation only contains fludioxonil and surfactans in substantial higher amounts (>2 times) than Sporgard WB so the effects of surfactants on the dermal absorption values seems to have been sufficiently addressed..
Sporgard WB contains about 2% w/w fludioxonil (about 20 g fludioxonil/L) and low levels of surfactants (total 4% w/w content) and fillers (3% w/w content) as co-formulants most likely to influence dermal absorption. There are no solvents present in Sporgard WB that could enhance absorption. The product studies on Sporgard WB further supported that the product is not a sensitizer or a local irritant.

As seen in the existing dermal absorption data the impact of co-formulants on dermal absorption seems low and the concentration of fludioxonil has a small effect on absorption; (in this case it seems also that the formulation type has a small impact). This is evident when comparing the total dermal absorption values too *in vitro* studies on human epidermis performed in the same laboratory, same/similar concentration of fludioxonil tested and in the same time period by the same author on two different formulation (Fludioxonil 230 g/l SC formulation & Fludioxonil/cyprodinil 62.5 WG). For Fludioxonil 230 g/l SC formulation the dermal absorption after 6 hours was 2.7% for the dilution and 0.2% for the

concentrate while for Fludioxonil/cyprodinil 62.5 WG dermal absorption was 2.58% for the dilution and 0.12% for the concentrate.
These figures are also in line with the calculated *in vivo* human dermal absorption values based on the three studies performed on Fludioxonil/cyprodinil 62.5 WG (EFSA conclusion).

Due to the above reasoning regarding similarities of formulation types and the remark regarding the EFSA calculation, the *in vitro* study on human epidermal membranes performed with Fludioxonil 230 g/l SC formulation seems to be the most accurate one to extrapolate from. Human skin samples also provides the best estimate. The maximum in use concentration range from 0.010-0.032% fludioxonil and the minimum concentration in the study tested was ~0.05 % fludioxonil. However the difference is considered to be minimal (all exposure calculation has only been performed maximum in use concentration) and taken into consideration that dermal absorption values are estimates and not exact values with possibility of rounding, normal risk of errors in laboratory testing and tape stripping techniques etc. it seems justified to consider these as similar concentrations.An overall dermal absorption value of 3% taken from the diluted fludioxonil SC formulation is considered to represents worst case used for both the concentrate and dilution (or in use concentrations).

With respect to the presents of other active substances in the formulations the EFSA guidance document section **6.5 Formulations containing more than 1 active substance** states the following
"Dermal absorption of active substances from combined formulations can be considered to be independent of the other active substances provided that none of the active substances is a significant irritant and/or sensitiser." The product studies on Sporgard WB supported that the product is not a sensitizer or a local irritant.

For risk assessment purposes, a dermal absorption value of 3% has been used for fludioxonil (all human exposure assesments have only been performed by using the maximum in use concentration of 0.032% fludioxonil). It should be noted that this is value is conservative when considering dermal absorption from end-use products such as paints, plaster-board and mineral sealants, where the active substance is expected to be bound in a matrix within the treated product or article. For the end used products is has been common praxis for other biocidal substances in e.g PT8 to use, as a worst case, the data from a solution. Composition of treated articles is known e.g. incorporation into paper or gypsum materials for the construction of wallboard- these are solid matrices which will expect to inhibit release of fludioxonill, or paint which is a largely aqueous matrix - containing pigments and filler that bind fludioxonil to the end coating. In both cases the availability of fludioxonil from treated articles is highly restricted compared to the Sporgard WB formulation. The existing dermal absorption conclusion (3%) is sufficiently conservative.

Value(s) used in the Risk Assessment – Dermal absorption	
Value(s)*	Dilution (0.05% fludioxonil)= 3 % (6 hr) ** 6 *In vitro* dermal absorption of fludioxonil through human epidermis. Fludioxonil 230 g/l SC formulation ([redacted]). Davies D J. 2005.
Justification for the selected value(s)	Please refer to extensive reasoning above in the text.

* the figures have been extrapolated from a study on a SC formulation to a WB formulation. Comparable dilutions with fludioxonil content between 0.05%- 23% a dermal absorption of 3% would be justified while comparable concentrates with a fludioxonil content ≥23 % a dermal absorption of ~0.2% could be used.

** the dermal absorption value is applicable for the active substance and might not be usable in product authorization. Also these are also only applicatable for the maximum in use concentration ranges which has been used in the exposure assessment.

3.1.2 Values and conclusions used for the risk assessment

ADME

About 80 % of the high dose was absorbed from the gastrointestinal tract based on the data obtained for the bile duct fistulated animals. The absorbed material was rapidly excreted with about 13-20% % in the urine and about 78-83 % in the faeces within 24 hours. The excretion was mainly via the bile (68%) and there was evidence for a degree of enterohepatic recirculation. Considering the residual carcass radioactivity in cannulated rats and based on the characterisation of metabolites, the total systemic availability of fludioxonil is likely to be in excess of 80% at the high dose level and is likely to be almost quantitative at low dose levels. At the time to maximal blood concentration (0.5 hours) the tissue concentrations were below 0.05 ppm equivalents except in liver, kidneys, lungs and plasma and declined rapidly. Residues were low in all tissues, but were comparatively high in the liver and kidney, reflecting biliary and urinary excretion. As a consequence of the rapid elimination from tissues, no accumulation or retention of the test substance and/or its metabolites is expected. Tissue distribution appeared to be largely independent of sex and dose.

The excretion rate and route was independent of the sex and dose level.
The metabolite pattern was complex but appeared to be independent of sex, dose level, and pre-treatment. Unchanged fludioxonil was detected in faeces as the only identified component but was not found in the urine.

Value(s) used in the Risk Assessment – Dermal absorption	
Value(s)*, **	3% for both the concentrate and in use concentrations *In vitro* dermal absorption of fludioxonil through human epidermis. Fludioxonil 230 g/l SC formulation ([redacted]). Davies D J. 2005.
Justification for the selected value(s)	Please refer to extensive reasoning above.

* the figures have been extrapolated from a study on a SC formulation to a WB formulation. Comparable dilutions with fludioxonil content between 0.05%- 23% a dermal absorption of 3%

would be justified while comparable concentrates with a fludioxonil content ≥23 % a dermal absorption of ~0.2% could be used.

** the dermal absorption value is applicable for the active substance and might not be usable in product authorization. Also these are also only applicatable for the maximum in use concentration ranges which has been used in the exposure assessment.

3.2 ACUTE TOXICITY

3.2.1 Acute oral toxicity

Summary table of animal studies on acute oral toxicity						
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance (purity%) Dose levels, Type of administration** *(gavage, in diet, other)*	**Signs of toxicity** *(nature, onset, duration, severity, reversibility)*	**Value LD_{50}**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 401 (1987), GLP, 1	Rat Sprague Dawley SD five/sex	Fludioxonil ([redacted]) Limit test: 5000 mg/kg bw Gavage	Soft faeces in half of the animals on the day of treatment	>5000 mg/kg bw	None	[redacted], 1991a (IUCLID 8.7.1-01)

The only clinical sign recorded was soft stool in half of the animals on the day of dosing. All animals appeared normal on the following day. No deaths occurred during the observation period. Bodyweight gain was unaffected by treatment. No visible lesions were observed in any test animal at necropsy. The acute oral LD_{50} of fludioxonil in the rat was found to be >5000 mg/kg bw under the conditions of this study.
No classification for fludioxonil is warranted for acute oral toxicity in accordance with Regulation (EC) No 1272/2008.

No human data is available.

3.2.2 Acute dermal toxicity

Summary table of animal studies on acute dermal toxicity					
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance (purity%), Vehicle, Dose levels, Surface area,**	**Value LD_{50}**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 402 (1987), GLP, 1	Rat Tif:RAI f (SPF) Five/sex	Fludioxonil ([redacted]), Distilled water contain 0.5% carboxymethylcellulose and 0.1% polysorbate 80 Limit test 2000 mg/kg bw. >10% of body surface; intact skin dermal	>2000 mg/kg bw	None	[redacted]., 1988 (IUCLID 8.7.3-01)

No deaths occurred. Signs of toxicity (piloerection, hunched posture, ventral recumbency and dyspnoea) were observed in all animals and persisted for up to six days. Weight loss was observed in two males and one female during week 2, however all animals gained weight over the study period. Gross necropsy did not reveal any treatment-related findings.

The acute dermal LD_{50} of fludioxonil in the rat was found to be >2000 mg/kg bw under the conditions of this study.
No classification for fludioxonil is warranted for acute dermal toxicity according to Regulation (EC) No 1272/2008.

No human data is available.

3.2.3 Acute inhalation toxicity

Summary table of animal studies on acute inhalation toxicity					
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance (purity%), Form, and particle size** *(MMAD)* **Actual and nominal concentration, Type of administration** *(nose only / whole body/ head only)*	**Value LC_{50}**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 403 (1981), GLP, 1	Rat Tif:RAIf (SPf) hybrids of RII/1 x RII/2 Five/sex	Fludioxonil ([redacted]) Dust/solid aerosol (MMAD 2.2 and 2.4 µm/1.6 µm GSD) 2.636 mg/ m^3 and 4022 mg/ m^3 Nose only	>2.636 mg/l (4 h, nose only)	None	[redacted]., 1989 (IUCLID 8.7.2-01)

No deaths occurred. Signs of toxicity in exposed rats included piloerection, hunched posture and dyspnoea. All treated animals appeared normal by Day 5. Reduced weight gain was apparent in exposed males. No signs of toxicity were observed in the control animals.

The acute inhalation LC_{50} of fludioxonil in the rat was found to be >2.636 mg/l under the conditions of this study. The tested concentration is stated to have been the maximum technically achievable. No classification is warranted for acute inhalation toxicity according to Regulation (EC) No 1272/2008.

No human data is available.

3.2.4 Overall conclusion on acute toxicity

Fludioxonil was found to be of low toxicity via the oral, dermal and inhalation routes. The acute oral LD_{50} was >5000 mg/kg bw; signs of toxicity were limited to soft faeces on the day of dosing. The acute dermal LD_{50} of fludioxonil was found to be >2000 mg/kg bw; piloerection seen in this study persisted to Day 6. The acute inhalation LC_{50} of fludioxonil was higher than the maximum achievable concentration of 2.636 mg/L.

No classification is therefore required for acute oral, dermal and inhalation toxicology, according to Regulation (EC) No 1272/2008.

3.3 IRRITATION AND CORROSION

3.3.1 Skin corrosion and irritation

Summary table of animal studies on skin corrosion/irritation					
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance (purity%), Vehicle, Dose levels, Duration of exposure**	**Results** *Average score (24, 48, 72 h)*	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 404 (1992), GLP, 1	Rabbit NZW m(3)	Fludioxonil ([redacted] No vehicle (gauze patch moistened with distilled water) 0.5 g fludioxonil/animal 4 hours (7 days post exposure period)	Erythema: 0.22 Oedema: 0.00 Very slight erythema in two rabbits at one hour and persisted to 48 hours in one animal.	None	[redacted].,1988a (IUCLID 8.1-01)

OECD 404 (1992), GLP, 1	Rabbit NZW 3/sex	Fludioxonil ([redacted]), No vehicle (0.9 % saline used for moistening the test substance) 0.5 g fludioxonil/animal 4 hours (7 days post exposure period)	Erythema: 0.00 Oedema: 0.00 No local dermal reactions were observed in any animal at any time point	None	[redacted]1991b (IUCLID 8.1-02)

Fludioxonil was found to be a non-irritant to the skin in one study and a minimal skin irritant (reactions of low severity and readily reversible) in a further study.

No classification is warranted for skin irritation according to Regulation (EC) No 1272/2008.

No human data is available.

3.3.2 Eye irritation

Summary table of animal studies on serious eye damage and eye irritation					
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance (purity%)** **Dose levels, Duration of exposure**	**Results** *Average score (24, 48, 72 h)*	**Remarks** *(e.g. major deviations)*	**Reference** **IUCLID section No**
OECD 405, GLP, 1	Rabbit, NZW, f(3)	Fludioxonil ([redacted]) 0.1 ml (31 mg) of fludioxonil 72 hours observations period after instillation	Conjunctival redness: .22 Conjunctival Chemosis: 0.00 Iridial & corneal effects: 0.00 There were no corneal or iridial reactions in any animal. Slight conjunctival redness was present in all three animals after 1 hour but had disappeared after 24 hours in one animal and after 48 hours in the remaining two animals. Slight conjunctival chemosis was observed in one animal at the 1-hour observation only.	None	[redacted], 1988b (IUCLID 8.2-01)

Fludioxonil was found to be a mild eye irritant under the conditions of this study; findings were limited to the conjunctivae and were reversible within 48 hours.
No classification for fludioxonil is warranted for eye irritation according to Regulation (EC) No 1272/2008.

No human data is available.

3.3.3 Respiratory tract irritation

No significant signs of respiratory tract irritation were observed in the acute inhalation study in rats. No subchronic inhalation studies have been submitted.

No human data is available for this end point.

3.3.4 Overall conclusion on corrosion and irritation

Skin irritation:

No skin irritation/corrosion or oedema but slight erythema (mean score of 0.22 for the 24-72 hours readings) in 2 of 3 male New Zealand white rabbits were observed in one study. In a second test no signs of irritation/corrosion, erythema or oedema were observed at any of the 1-72-hour readings in any of the 3 male and 3 female New Zealand white rabbits following a 4-hour semi-occluded application of undiluted fludioxonil. Fludioxonil is therefore not considered to be a skin irritant.

Eye irritation:

Slight redness (mean score of 0.22 for the 24-72 hours readings) of the conjunctival sac was seen in 2 of 3 female New Zealand white rabbits while no effects were observed on cornea or iris. Fludioxonil is not considered to be an eye irritant.

No classification is warranted for skin or eye irritation according to Regulation (EC) No 1272/2008.

3.4 SENSITISATION

3.4.1 Skin sensitisation

Summary table of animal studies on skin sensitisation					
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance (purity %), Vehicle, Dose levels, Route of exposure** *(topical/intradermal, if relevant)*, **Duration of exposure**	**Results** *(EC3-value or amount of sensitised animals at induction dose)*	**Remarks** *(e.g. major deviations)*	**Reference**
Skin sensitisation Maximization test (OECD 406, 1992) GLP, 1	Guinea pig (Tif:DHP) 10/sex 5/sex (control)	Fludioxonil ([redacted]) Vaseline 1% fludioxonil for intradermal induction 30% fludioxonil for topical induction 10% fludioxonil for topical challenge Intradermal and topical exposure 48 hr for induction 24 hr for challenge	0/20 animals in the test group showed any dermal reactions following challenge. No dermal reaction was observed in control animals either.	The challenge concentration of 10% active substance in vaseline is too low. A concentration of 30% fludioxonil did not induce mild-to moderate skin irritation and 10% can therefore not be said to be the highest non-irritant dose.	[redacted]., 1988c (IUCLID 8.3-01)

Skin sensitisation Maximization test (OECD 406, 1999) GLP, 1		Celest 025 FS containing 26 g Fludioxonil/l Physiological saline 5% for intradermal induction 80% for topical induction 5% for topical challenge Intradermal and topical exposure 48 hr for induction 24 hr for challenge	0/20 animals in the test group showed any dermal reactions following challenge.	-	[redacted]., 1999 (IUCLID 8.3-02)

The potential of fludioxonil to induce delayed contact hypersensitivity (skin sensitisation) was investigated in a Maximisation test using 10 test animals/sex and 5 control animals/sex. Test substance concentrations of 1% and 30% were used for intradermal and topical induction exposures, respectively. Local dermal irritation at the application site was induced using sodium lauryl sulphate prior to topical induction. Test and control animals were challenged using a concentration of 10% test substance. The challenge dose were considered to be low, this was also concluded in the EFSA conclusion report (Directive 91/414/EEC). This partially invalidates the study. No dermal reactions were observed in test or control animals following the challenge exposure: no evidence of sensitisation was seen under the conditions of this study
However further confirmatory data is needed to draw the final conclusion regarding skin sensitisation. Therefore CA DK requested during the evaluation period the study done on the formulation Celest 025 FS – containing 26 g Fludioxonil/l which was also submitted for the PPP review process.

In the Maximisation test performed with the product Celest 025 FS – containing 26 g Fludioxonil/l delayed contact hypersensitivity was investigated using 10 test animals/sex and 5 control animals/sex. At pre-test, irritation was produced after intradermal induction with concentrations from 0.5 % - 5 % in physiological saline and after epidermal application of concentrations from 10 % - 100 % (vehicle physiological saline) in both male and female

guinea pigs. Concentrations selected for the maximisation test was 5 % test material and 80 % test material with physiological saline for intradermal and topical induction, respectively, and 5 % test material in physiological saline was selected for epidermal challenge.
It was not possible to document irritation by the test material during epidermal induction (no depilation) due to the colouring properties of the test material. There were no positive skin reactions following epidermal challenge with test material or physiological saline either at the 24-hour or the 48-hour readings in either of the test substance group or the control group animals. There were no mortalities in the test and the treatment did not affect the body weight or the body weight gain. In conclusion Celest 025 FS is not considered to be a skin sensitiser under the experimental condition in the performed study.

No human data is available.

3.4.2 Respiratory sensitisation

No animal or human data are available. Currently no recognised test guidelines exist for this end point.

3.4.3 Overall conclusion on sensitisation

Two studies ([redacted]., 1988c & [redacted]., 1999) has been submitted to evaluate the sensitisation potential of fludioxonil.

The challenge concentration of 10% in the first study ([redacted]., 1988c) was regarded to be too low. The study is considered acceptable, but the OECD guideline was not fulfilled referring to the levels of doses selected. This might partially invalidate the study. However, a second study [redacted]., 1999) is available with a formulation containing only one active substance, showing negative results.
Taking into account all evidences, no sensitising potential is expected for fludioxonil.
This is also in line with the conclusion of the EFSA conclusion report for fludioxonil evaluated under Directive 91/414/EEC.

3.5 SHORT TERM REPEATED DOSE TOXICITY

3.5.1 Short-term oral toxicity

Summary table of oral short-term animal studies (usually 28-day studies)							
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance Dose levels, Route of exposure Duration of exposure**	**NOAEL,** males/ females mg/kg bw/day	**LOAEL** males/ females mg/kg bw/day	**Critical effects**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 407 GLP, 1	Rat Tif:RAIf (SPF) 10/sex	Fludioxonil ([redacted] Oral 0, 10, 100, 1000 mg/kg 28 day	100	1000	Effects on bodyweight, clinical chemistry increased liver weights and hepatocyte hypertrophy; increased kidney weight and associated pathological changes including blood in urine.	Minor. The study is according to the guideline in force at the time	[redacted]., 1990 (IUCLID 8.9.1.1-01)

Under the conditions of the 28 days oral rat study no animals died and the only treatment related clinical observation was a blue discoloration of the tail in both sexes at the top dose level (1000 mg/kg bw day), associated with the excretion of the coloured metabolite SYN 518582. Body weight gain was minimally reduced in high dose males but did not reach statistical significance. The cumulative body weight gain (week 1-4) was 40% of control for high dose females and resulted in statistical significance reduction of 12% in final bodyweight compared to control. In high dose males the final body weigh was 9 % of control. The body weight of the other dose groups was unaffected. Food consumption was reduced throughout the study in 1000 mg/kg bw/day females and was marginally reduced in 1000 mg/kg bw/d males during Weeks 1 and 2. The mean food consumption (week 1-4) was 79% of control in high dose females and 96% of control in high dose males.
There was no effect on food consumption at the lower doses and no treatment-related effect on water consumption.
No treatment related significant effect were observed at the haematological parameters.
In clinical chemistry glucose levels were statistically significantly reduced in high dose (1000 mg/kg bw day) females and males and at 100 mg/kg bw day in females only. At 100 mg/kg bw/day no relevant correlates on liver parameters, bodyweight development or food consumption were observed

and therefore no toxicological significance is attributed to the marginally lower glucose levels in males at this dose level. Plasma cholesterol was statistically significantly increased in both sexes at the high dose and in females at 100 mg/kg bw day. The effects on plasma cholesterol at 100 mg/kg bw day is considered of less toxicological significance since it is within the historical controls (HCD data are verified; [redacted]). Bilirubin levels were increased (statistical significance) at high dose females.
Treatment related changes in liver and kidney weight (increase in relative and/or absolute) were observed in both sexes at high dose. The increase at 100 mg/kg bw day in females on these organs (absolute and relative liver weight and relative kidney weight) were not associated with any histopathology or clinical chemistry correlates indicating liver or kidney damage and therefore not considered adverse. Histopathology revealed increased incidences of hepatocyte hypertrophy in both sexes at the top dose level and renal tubular casts in males at the top dose level. In urine ketones were found in all dose groups (no clear dose-response relationship) for males and in the two high dose groups in females. The historical controls reveals a general high incidence (HCD data are verified; [redacted]) for this effect and were within the historical control data. Ketones in urine is normally a manifest of glucose shortage (as indication of shift to a alternative source of energy) however glucose levels, body weight development or food consumption were not generally decreased or affected except in high dose animals. The toxicological significance of this finding is unclear. In two high dose males blood was found in the urine.

Conclusion:
Fludioxonil produced hepatotoxicity (increased liver weights and hepatocyte hypertrophy) and nephrotoxicity (increased relative kidney weight and pathological changes including blood in urine) in the highest dose group (1000 mg/kg bw/day) indicating liver and kidneys as target organs. Metabolic changes indicated by changed biochemical and urinalysis parameters (decreased glucose, increased incidence of ketonuria) were recorded in high-dose animals as well. The NOAEL is considered to be 100 mg/kg bw/day for both males and females with a LOAEL of 1000 mg/kg bw/day. The increase in the relative kidney weight in females at 100 mg/kg/day is not considered adverse as the increase is small and no clear dose-response relationship was seen. The increase in liver weight in females at 100 mg/kg bw/day is not considered adverse either as there are no other effects on the liver at this dose.

No human data is available.

3.5.2 Short-term dermal toxicity

Summary table of dermal short-term animal studies (usually 28-day studies)							
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/ group**	**Test substance, Vehicle Dose levels, Surface area, Duration of exposure**	**NOAEL,** males/ females mg/kg bw/day	**LOAEL** males/ females mg/kg bw/day	**Results**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 410 (1981) GLP, 1	Rat Tif:RAIf (SPF) 5/sex	Fludioxonil ([redacted]) 0, 40, 200 and 1000 mg/kg bw/day Dermal 28 day	1000/200	-/1000	phagocytic cells in the thymus in all females	None relevant	[redacted]., 1990 (IUCLID 8.9.1.3-01)

In the dermal 28 days study in rats no treatment relevant effect were observed on mortality, bodyweight development, organ weights, food consumption, blood parameters (haematology) and no clinical or local dermal irritation signs.

Statistically significant higher plasma creatinine level in males at 1000 mg/kg bw/d and in females at the two top doses. The group mean and the individual values were however well within the historical control range (the historical control data was taken from 28 -day dermal studies performed in the same test facility in Tif-rats in 1988-1992; the initial bodyweight matched the bodyweights of the study with fludioxonil. the minimum and maximum values reported are the minimum and maximum of individual values) and (in females) do not form a dose-response relationship. Findings are therefore not considered to be toxicologically relevant.
Minor (but statistically significant) increases in plasma globulin and total protein levels were seen in females at 200 and 1000 mg/kg bw/d. However the group mean values and the individual values are well within the historical control range and do not form a dose-response relationship; the variations are therefore not considered to be treatment-related or toxicologically relevant. This was also the conclusion from the expert meeting when the substance was evaluated as a pesticide (Directive 91/414/EEC).

The only histopathological change considered to be treatment-related was enlarged cortical macrophages - often revealing lymphophagocytosis - in the thymuses of 1000 mg/kg bw/d females. No relevant thymus effects in all other studies with fludioxonil in rats or other species was observed for fludioxonil, however the toxicological significance of the thymus findings is unclear (all females) and a NOAEL of 200 mg/kg bw day is therefore supported in this study.

Conclusion:
Under the experimental conditions of this OECD guideline no. 410 study in albino rats of the Tif:RAIf strain exposed by dermal application (6 hours per day, 5 days per week, 4 weeks) to 97.5 % pure fludioxonil at dose levels of 0, 40, 200 or 1000 mg/kg bw/day the thymus of all of the highest dose group females showed enlarged cortical macrophages and often revealed lymphophagocytosis. The NOAEL is considered to be 200 mg/kg bw/day based on the effects observed in the thymus of high-dose females. For males, the NOAEL is 1000 mg/kg bw/day.

No human data is available.

3.5.3 Short-term inhalation toxicity

No inhalation data is available. Fludioxonil is not volatile and is of low acute toxicity by the inhalation route (LC50 >2.636 mg/l; [redacted], 1989). The proposed use of the biocidal products will not result in significant exposure by the inhalation route. A short-term inhalation study is not necessary.

3.5.4 Overall conclusion on short-term repeated dose toxicity

The repeated oral short term study indicated the target organs to be liver and kidney in rats with NOAEL of 100 mg/kg bw/day for both males and females with a LOAEL of 1000 mg/kg bw/day.

The repeated **dermal short term** study in **rats** pointed at the thymus as a target organ as all high-dose females had enlarged macrophages in the thymic cortex and often lymphophagocytosis with a NOAEL of 200 mg/kg bw day and LOAEL of 1000 mg/kg bw day. This effect was not observed in males and resulted in NOAEL 1000 mg/kg bw day (top dose).

No classification based on the effects seen in these two studies is required according to Regulation (EC) No 1272/2008.

3.6 SUB-CHRONIC REPEATED DOSE TOXICITY

3.6.1 Sub-chronic oral toxicity

	Summary table of oral sub-chronic animal studies (90-day studies)						
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/ group**	**Test substance** **Dose levels,** **Route of exposure** **Duration of exposure**	**NOAEL,** males/ females mg/kg bw/day	**LOAEL** males/ females mg/kg bw/day	**Results/critical effects**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 408 (1998) GLP, 1	Rat Sprague Dawley 10/sex	Fludioxonil ([redacted]) 0, 10, 100, 1000, 7000, or 20000 ppm* Oral 90 day	64 / 70	428/462	Effects in the kidney and liver at the two highest dose groups in both sexes (increased relative weights, chronic nephropathy, centrilobular hepatocyte hypertrophy)	None	[redacted].1990 (IUCLID 8.9.1.1-02)
OECD 409 (1981) GLP, 1	Dog Beagle 6/sex (0 & 15000/1000 ppm) 4/sex (200& 2000 ppm)	Fludioxonil ([redacted]%) 0, 200, 2000 or 15000 ppm (day 1 to day 17)/10000 ppm (day 18-the end of study)** Oral 13 weeks (28 days recovery)	60/58.5	299/351	Decreased body weight in high-dose animals, increased a/r liver weight and histopathological changes in high-dose animals, bile duct proliferation, signs of mild anaemia in high-dose females.	The animals were 2 months too old at study start	[redacted]., 1990 (IUCLID 8.9.1.1-03)

OECD 452 GLP, 1	Dog Beagle 4/sex	Fludioxonil (97.5%) 0, 100, 1000 or 8000 ppm*** 12 months	33/35.5	298/331	Weight loss (m), reduced bw gain, increased relative liver weight (m/f), increased cholesterol (m), gross and histopathology (m/f) in high dose	-	[redacted] 1992, 1994 (amendment No. 3 including historical controls) (IUCLID 8.9.1.1-08)

** The mean achieved dose levels of fludioxonil were calculated to be 0.8 and 1.0, 6.6 and 7.1, 64 and 70, 428 and 462, 1283 and 1288 mg/kg bw/d for males and females at 10, 100, 1000, 7000 and 20000 ppm respectively.*
*** The dietary doses of 200, 2000 and 10000 ppm were equivalent to 6.16, 60.0 and 299 mg/kg bw/day in males and 5.90, 58.5 and 351 mg/kg bw/day in females (calculated by Syngenta).*
**** The dietary doses of 100, 1000 and 8000 ppm were equivalent to 3.1, 33.1, 298 mg/kg bw/d (males) and 0, 3.3, 35.5, 331 mg/kg bw/d (females).*

In the **90 days oral Sprague Dawley rat study** two deaths occurred among treated males; one rat at 20000 ppm was found dead on day 36 and one rat at 7000 ppm was sacrificed on day 50 in moribund condition (caused by a pituitary adenoma). These deaths are not considered to be a result of dosing. Treatment related clinical signs were limited to blue staining of the tail, abdomen, feet and perineum started on day 6-14 in the two high dose groups. The blue staining was associated with the urinary excretion of a coloured metabolite and not considered to be of toxicological significance.

Body weights and body weight gains were statistically significantly decreased in both sexes at 20000 ppm (from week 1) and in females at 7000 ppm as well (from week 4). The relative decrements for the body weight gains were 3 %, 14 %, and 41 % (males), and 6 %, 33 %, and 61 % (females) for the 1000 ppm, 7000 ppm and 20000 ppm dose groups, respectively. No effects were observed at the two lowest doses compared to control animals. Food consumption was statistically significantly decreased in male rats at 20000 ppm and in female rats from 7000 ppm throughout the study. Significant decreases in feed efficiencies occurred early in the study in both sexes at the highest dose.
Haematology revealed treatment-related statistical significance effects on erythrocyte parameters in females at 7000 and 20000 ppm; similar effects were not apparent in males. In the clinical chemistry investigations indication of liver and kidney toxicity were observed in both sexes at 20000 ppm and liver toxicity (↑cholesterol, ↑bilirubin & ↓5'nucleotidase) at 7000 ppm. Discoloration of urine samples were noted at ≥1000 ppm; this finding is consistent with the excretion of the coloured metabolite SYN 518582. Urine volumes were lower in females at 7000 and 20000 ppm; significant amounts of bilirubin were detected in urine samples from both sexes at these dose levels.

Statistically significant differences between treated and control group animals were observed for a number of organ weights in the two highest dose groups with increased relative kidney and liver weights being the most prominent findings . These changes were consistent with the microscopically identified changes in the liver (centrilobular hepatocyte hypertrophy) and in the kidneys (chronic nephropathy followed by a prominent active inflammatory component) of animals at the two highest dose levels. An increased incidence (not statistically significant) of slight centrilobular hepatocyte hypertrophy was seen in males at 1000 ppm. It is the opinion of the eCA that the effect is a biologically significant effect. Furthermore, the incidence of centrilobular hepatocyte hypertrophy in males at 1000 ppm (5/10) is borderline to a statistically significant difference as the incidence (6/10) in 7000 ppm females is statistically significantly different from the incidence in the control group (Fisher's exact test with Bonferroni correction). However in the absence of any association with clinical chemistry or additional histopathological parameters in this study and compared with the results in the 2 year rat study where no histopathological changes were observed in the liver of animals given 1000 ppm the finding is not considered to be of toxicological significance. Therefore, the NOAEL for liver effects is considered to be 1000 ppm.

Conclusion:
90 days oral exposure for fludioxonil in Sprague Dawley rats resulted in clinical signs of toxicity, reduced body weight and body weight gain, haematological effects (females only), changes in clinical biochemistry, differences in a number of organ weights, gross necropsy findings, and histopathological changes consistent with kidney and liver damage in males and females in the two highest dose groups. The same kind of histopathological changes in the liver and kidneys were also observed at 1000 ppm although the incidences were not statistically significantly different when compared with the control group. A NOAEL of 1000 ppm corresponding to 64 mg/kg bw/day for males and 70 mg/kg bw/day for females is set based on the histopathological changes observed in the liver and kidneys from 7000 ppm (428 mg/kg bw day).

In the **13 weeks oral dog study** (28 days recovery period) dogs were initially given 0, 200, 2000 and 15000 ppm fludioxonil. The high dose level of 15000 ppm was reduced to 10000 ppm on Day 18 due to

marked body weight loss in both sexes during the first three weeks of treatment with 15000 ppm and the body weights were consequently stabilised. No deaths occurred in any of the groups. A statistically significantly decreased body weight was noted in high-dose males from week 4 and throughout the feeding period; in females the bodyweight was 90 and 87% of control at week 8 and 14 in the high dose. During the recovery period no body weight gain was noted in high dose animals of either sex.
Food consumption was normal in animals administered 200, 2000 and 10000 ppm diet, but was decreased (approximately 50 %) in both sexes during the 17 days of feeding with the 15000 ppm diet.

There were no significant differences between control and treatment groups with respect to food consumption.

Diarrhoea was observed with increased frequency (number of observations and number of animals affected) in both sexes at 2000 and 10000 ppm, although the general condition of the animals was not impaired. The relevance of the diarrhoea effect was discussed at an expert meeting when the substance was evaluated under PPP and the meeting agreed that the effect was treatment related but not adverse. This was based on the fact that the incidence of diarrhoea was episodically and transient and the same effect was not seen in a 1 year dog study at doses from 1000 ppm to 8000 ppm performed in the same laboratory with dogs from the same source. According to incidence data it was clear, that the diarrhoea occurred episodically at 2000 ppm in 3/4 females and 3/4 males for average of 7 days for males and 5 days for females. Therefore the CA is of the opinion that the diarrhoea at 2000 ppm should not be considered as an adverse effect.

Ophthalmoscopy did not reveal any effects of treatment.

Statistically significant changes in fibrinogen concentration and platelet count at the high dose level are not considered to be clearly related to treatment as the individual values are within the range of historical controls. However it is noted that the age of animals for historical control data (6-9 months) is less than that of the animals in this study (11 months old at study initiation). A relation to treatment cannot therefore be excluded completely.
Treatment-related effects were limited to an statistical significance increase in cholesterol concentration in high dose females at Weeks 4, 8 and 13, which was reversible during the recovery period. A trend for increased cholesterol concentration was also observed in individual high dose males at Weeks 8 and 13.
Urinalysis did not reveal any effect of treatment.
There was an increased (no statistic was performed on organ weights) in the absolute and relative liver weights in both sexes at 15000/10000 ppm. Gross necropsy did not reveal any findings of toxicological significance and effects were limited to staining of the gastro-intestinal tract at the high dose level, consistent with the excretion of a coloured metabolite. Histopathological findings were limited to a increased incidence in the severity of bile duct hyperplasia in both sexes at the high dose level. Overall at the end of the recovery period there was indication of reversibility with respect to changes recorded.

Conclusion:
Under the conditions of this 90-day feeding study in male and female Beagle dogs (followed by 28-days recovery for some control and high dose animals) administration of 0, 200, 2000 or 15000/10000 ppm caused episodically and transient diarrhoea and blue coloured faeces in the mid-dose group (3/4 animals of both sexes) and in all high-dose animals, decreased body weight in the high-dose group (males), signs of mild anaemia in high-dose females, and increased absolute and relative liver weights in high-dose animals. These increased liver weights corresponded to increased severity of bile duct proliferation in high-dose animals. The NOAEL is considered to be 2000 ppm, equivalent to 60 mg/kg bw/day in males and 58.5 mg/kg bw/day in females. As the diarrhoea in mid dose animals were transient and did not correlate with other effects as e.g. bodyweight development, this effect is not considered adverse. In the high dose group there was decreased body weight gain and mild anaemia in the females. There was an indication of reversibility for the noted changes at the end of the 28-day recovery period.

In the **12 months oral dog study** dogs were dosed with 0, 100, 1000 and 8000 ppm fludioxonil no deaths occurred in any control or treated group.
Clinical signs were limited to blue faeces in both sexes at the high dose only, consistent with the excretion of a coloured metabolite.
At 8000 ppm a mean body weight loss of 0.4 kg was recorded after 52 weeks of treatment while the body weight gain in low- and mid-dose males exceeded that of the male control group. The body weight gain in low-dose females were similar to that of the female control group whereas females at 1000 ppm gained 43 % less weight and high-dose females gained 51 % less weight during the study period (differences not statistically significant).
No corresponding significant effects were seen on food consumption.
All haematological values were minimally changed in relation to control group data and within the normal range of the historical control data for the performing laboratory (1989-1992). In the clinical chemistry parameters a statistically significant increase in total cholesterol was observed in males at 8000 ppm. However all other clinical biochemistry parameters and urinalysis the values were within the historical control values for the performing laboratory.
A statistical significant increase in the absolute (14%) and relative (36%) liver weight in females at 8000 ppm were observed while in males also at the top dose an statistical significanct increase was only seen in the relative (28%) liver weight. The increased relative liver weight observed for high-dose animals was in accordance with the liver enlargement noted at the gross necropsy examination for 2 of 4 high-dose females (2/4 high-dose females had enlarged livers and a greenish deposit was found in the mucosa of the caecum, colon or rectum in 3/4 males and 2/4 females from the high-dose group) but was not confirmed in the histopathological examination.
A number of other findings were recorded with same incidence in control and low-, mid- and high-dose groups.
Histopathology revealed a single incidence of biliary epithelial cell proliferation in females at 8000 ppm.

Conclusion:
Under the conditions of this study in male and female Beagle dogs administered 0, 100, 1000 or 8000 ppm Fludioxonil in the diet for one year the NOAEL is considered to be 1000 ppm corresponding to 33.1 mg/kg bw/day in males and 35.5 mg/kg bw/day in females due to body weight loss (m), reduced body weight gain (f/m), increased relative liver weight in high-dose animals (f/m), gross pathology and histopathology (f) and increased total serum cholesterol (m) at the highest dose of 8000 ppm (LOAEL).

No human data is available.

3.6.2 Sub-chronic dermal toxicity

No data is available.

3.6.3 Sub-chronic inhalation toxicity

No data is available.

3.6.4 Overall conclusion on sub-chronic repeated dose toxicity

A total of 3 oral studies (dietary) were available for the evaluation of the toxicity of fludioxonil in rats and dogs.

The studies indicate that repeated **oral** administration of fludioxonil is toxic to the liver of rats and dogs, and to the kidney of rats.

Signs of hepatotoxicity include increased organ weights (rats and dogs) and histopathological changes (centrilobular hepatocyte hypertrophy in rats, bile duct proliferation in dogs).
According to results in 90-day studies in rats indicated similar sensitivity for both sexes regarding hepatocyte hypertrophy.
It can be discussed whether the finding of centrilobular hepatocyte hypertrophy at 1000 ppm in the 90-day rat study is an adverse effect as statistically significance from the control group was not achieved (Fisher's exact test with Bonferroni correction). It is the opinion of the CA that the effect is a biologically significant effect. Furthermore, the incidence of centrilobular hepatocyte hypertrophy in males at 1000 ppm (5/10) is borderline to a statistically significant difference as the incidence (6/10) in 7000 ppm females is statistically significantly different from the incidence in the control group (Fisher's exact test with Bonferroni correction). However in the absence of any association with clinical chemistry or additional histopathological parameters in this study and no histopathological changes were observed in the liver of animals given 1000 ppm in the 2-year rat study the finding is not considered of toxicological significance. Therefore, the NOAEL for liver effects is considered to be 1000 ppm.
Signs of nephrotoxicity include increased organ weight (relative to body weight in rats) and histopathological changes (nephropathy in rats).

Another target organ identified in the short term oral studies includes the haematopoietic system (signs of mild anaemia in female dogs). The two dog studies available for evaluation (a 90-day dietary study with 28 days recovery and a one-year dietary study) indicates that the liver is a target organ (increased relative weight in both studies and histopathological changes (bile duct proliferation and portal fibrosis) in the 90-day study. These effects were observed at 10000 ppm in the 90-day study and 8000 ppm in the one-year study. Other findings in the 90-day study included episodical diarrhoea from 2000 ppm and signs of mild anaemia in females at 10000 ppm. The 90-day study in dogs included a 28-day recovery period and there was an indication that the biological changes recorded in the high-dose animals were reversible within the 28-day recovery period.
The NOAEL is considered to be 2000 ppm (60/58.5 mg/kg bw day in males and females) in the 90 day dog study. In the one-year study, other findings included increased cholesterol in high-dose males; the NOAEL is 33.1/35.5 mg/kg bw/day in males and females, respectively.

Classification:
Based on the results of the two sub-chronic repeated dose studies no classification for effects by prolonged exposure via the oral route is warranted for fludioxonil according to Regulation (EC) No 1272/2008.

3.7 LONG-TERM REPEATED DOSE TOXICITY

3.7.1 Long-term oral toxicity

Summary table of oral long-term animal studies							
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/ group**	**Test substance** **Dose levels,** **Route of exposure** **Duration of exposure**	**NOAEL,** males/ females mg/kg bw/day	**LOAEL** males/ females mg/kg bw/day	**Results/critical effects**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 453 GLP, 1	Rat Sprague Dawley 50 sex/group	Fludioxonil ([redacted] 0, 10, 30, 100, 1000, or 3000 ppm* 24 months	Chronic: 37/ 44 Carcinoge-nicity: 113 / 141	Chronic: 113/141 Carcinoge-nicity: - / -	high dose: Reduced weight gain and body weight Signs of slight anaemia (females) Liver: degenerative changes; kidney: nephropathy, cysts (males) -	Survival less 50% after 2 years, 7 weeks old rats at study start (not 6 weeks or younger as recommended)	[redacted] (1993c). (IUCLID 8.9.1.1-07)

OECD 451 GLP, 1	Mice Crl:CD®-1 (ICR) BR. 10 /sex/group (12 month, interim sacrifice) 50 sex/group (18 months)	Fludioxonil ([redacted] 0, 3, 10, 30 100, 1000, 3000, 5000, or 7000 ppm ** 18 month	Chronic: 112 / 133 Carcinoge-nicity: 851 / 1008	Chronic: 360 / 417 Carcinoge-nicity: - / -	Survival markedly reduced at 7000 ppm, body weight and body weight gain decreased from 5000 ppm, signs of anaemia at 7000 ppm, increased liver weight from 3000 ppm, bile duct hyperplasia at 7000 ppm (males), nephropathy from 5000 ppm.	MTD exceed at 7000 ppm	[redacted] (1993a & 1993b). (IUCLID 8.9.1.1-05 & 8.9.1.1-06)

** Mean achieved fludioxonil intakes were calculated to be 0.37 and 0.44; 1.1 and 1.3; 3.7 and 4.4; 37 and 44; 113 and 141 mg/kg bw/d for males and females at dose levels of 10, 30, 100, 1000 and 3000 ppm respectively.*

*** Mean achieved daily fludioxonil intakes were 0.41, 1.4, 4.1, 13.5, 133, 417, 715 and 1008 mg/kg bw day for females and 0.33, 1.1, 3.3, 11.3, 112, 360, 590 and 851 mg/kg bw day for males at dose levels of 3, 10, 30 100, 1000, 3000, 5000, or 7000 ppm, respectively.*

In the **two years oral combined chronic and carcinogenicity study in Sprague Dawley rats** there was no treatment related effect on survival. However the survival was generally low in both control and treated animals and is below the required survival according to OECD TG 453 but acceptable according to the EPA guideline. The survival of high-dose animals at 24 months was generally higher than that at the lower dose levels and the control group and varied between 28 and 36 % in male carcinogenicity groups and between 28 and 42 % in female carcinogenicity groups. At 18 months, survival was at least 76% in all groups. With the exception of animals administered 30 ppm, survival was close to 50% at Week 96 and was between 28-42% at 24 months in animals assigned to the oncogenicity phase. The lower survival became apparent towards the end of the study and is considered to be secondary to obesity, an effect common in this strain of rat. This would also explain the slightly higher survival in animals at 3000 ppm, which had slightly lower bodyweights. All animals dying prior to scheduled sacrifice were subjected to full necropsy and histopathological evaluation, and the incidence of neoplastic lesions determined. Therefore a sufficient number of animals were investigated for neoplastic lesions in the later phases of the study (either close to or at the scheduled terminal sacrifice) to allow a robust evaluation of the carcinogenic potential of fludioxonil.

Clinical signs were limited to slightly increased frequency of diarrhoea was seen in high dose males. Dark faeces, blue urine and blue staining on various areas of the body seen in both sexes at dose levels of ≥1000 ppm was not considered of not of toxicological significance, as they can be attributed to the presence of the blue-coloured metabolite SYN 518582.

At the high dose a reduced weight gain resulted in reduced absolute bodyweight of 5% and 11% lower than controls at 1 year for males and females, respectively; 5% and 8% lower at termination. Bodyweights of males and females at this dose level were significantly lower than controls from Week 51 and Week 5, respectively. Reductions in cumulative weight gain were 10% and 16% for males and females respectively at 12 months and 11% for both sexes over the whole treatment period. Cumulative bodyweight gain of 1000 ppm males was also slightly lower than controls during the first 13 weeks of the study, however mean bodyweights in this group were actually higher than controls at Week 13. The slightly lower weight gain in this group is therefore attributable to the slightly higher initial bodyweights of these animals and is not considered to be related to treatment.
Body weight gains were similar in control and high-dose group animals of both sexes during the recovery period.

Generally, food consumption was similar between control and treated groups of animals both during the study period and during recovery. No clearly treatment-related effects were apparent on food conversion efficiency.

There was no difference between water consumption in control and treated groups during the study.

With respect to haematological parameters changes in red blood cell parameters were primarily observed at the high dose at 12 months in females. Slight anaemia was observed in the high-dose females at 12 months as indicated by statistically significant decreases in red blood cell counts, haemoglobin, haematocrit, and mean corpuscular haemoglobin concentration. This decrease in red blood cell parameters was not observed at later sacrifices during the treatment period or at the 4-month recovery following 13 months of dosing. Other noted statistically significant differences between control and dosed groups in males or females throughout the study period were not considered as being treatment-related.

Clinical chemistry parameters were unaffected by treatment: occasional statistically significant effects are not considered to be treatment-related in the absence of any relationship to dose level or duration of treatment.

The only treatment-related change (dose and/or time response) in urinalysis was discoloration in the high-dose group, which is due to a coloured metabolite excreted in the urine and is not considered as being an adverse effect. The only additional effect of treatment was a slightly higher incidence of increased levels of urobilinogen seen at dose levels of ≥1000 ppm, findings attained statistical significance at 3000 ppm.

Organ weights was largely unaffected by treatment. Increases in the absolute weights of a small number of organs were seen in females, but are considered to be secondary to variations in bodyweights in the respective sub-group of animals; similar effects were not seen on relative organ weights and no relationship to dose level or duration of treatment was apparent.

The gross necropsy findings that occurred with increased frequency included enlarged livers in high-dose males, kidneys with cysts(s) in males from 1000 ppm, and discoloured foci or generally discolouration in both sexes in the two highest dose groups. The discolouration is due to a coloured metabolite excreted via the kidneys in the urine and is not considered as being an adverse effect. At the microscopical examination the incidence of kidneys with cysts in males at 1000 ppm was lower than in the control group and in the high dose group (3000 ppm); therefore the macroscopical finding of an increased incidence of kidneys with cysts in males at 1000 ppm is not considered as being adverse. Non-neoplastic histopathological findings were observed in the livers (degeneration, atrophy, inflammation, and necrosis) of high-dose animals and in the kidneys (cysts and progressive nephropathy) of high-dose males.

For male rats the incidences of liver adenoma, carcinoma, and adenoma and/or carcinoma in the low dose (10 ppm) group were higher than in the control and the high dose group and the incidences did not exhibit a monotonic dose-response relationship. As a result, they are considered statistically not significant. The incidence of hepatocellular tumours (adenoma, carcinoma and combined) were slightly increased in females at the top dose level 3000 ppm, however incidences do not attain statistical significance and were well within the laboratory's historical control ranges and. The increased incidences in the liver adenoma and combined adenoma and carcinoma in high-dose females were not statistically significant after Bonferroni adjustment of the tail probabilities. The carcinoma incidence in the high dose females was not analysed statistically since the single occurrence was insufficient for evaluation. Neoplasms were observed as solitary nodules (there was no tumour multiplicity) and were not associated with other evidence of a proliferative hepatocellular response such as increases in foci of cellular alteration. In the absence of a dose-relationship, coupled with the fact that the incidences fall within the historical control range, the hepatocellular tumours seen in females at 3000 ppm are not considered to be related to treatment. Treatment with fludioxonil had no influence on the total incidence of neoplastic lesions or on the number of tumour-bearing animals
As the historical control data were presented in the original study report (seven studies conducted at [redacted]), CA assumes that it was conducted within the same time period, the testing facitities were the same. However the time interval needs to be confirmed by the original data owner of the study which is the obligation of the applicant to provide. [redacted].

Labelling indices for liver sections from 12-month interim sacrifice and 13-month recovery sacrifice stained with Proliferating Cell Nuclear Antigen (PCNA) methodology indicated no treatment related effects on cell proliferation in rats after treatment with fludioxonil for 12 months. Marginally increased labelling indices for females administered ≥ 1000 ppm were considered incidental due to lack of statistical significance and dose relation.

Based on the above considerations concerning absence or no clear dose-response, incidences being within the HCD and PCNA investigation the hepatocellular tumours observed in this study are not considered to be related to the treatment with fludioxonil.

Conclusion:
In this combined chronic toxicity/carcinogenicity study in Sprague Dawley rats administered dietary concentrations of 0, 10, 30, 100, 1000, or 3000 ppm fludioxonil technical for up to 2 years effects were noted in both sexes at the highest dose level and included reduced body weight and body weight gain, signs of mild anaemia in females, gross necropsy and histopathological findings in the liver (both sexes) and the kidneys (males only). A slightly increased incidence of renal cysts seen in males at 1000 ppm is not considered to be of toxicological significance as this finding was not confirmed histopathologically. The NOAEL for chronic toxicity is considered to be 1000 ppm corresponding to 37 mg/kg bw/day in male rats and 44 mg/kg bw/day in female rats.
Fludioxonil was not carcinogenic in male or female rats at dietary doses up to 3000 ppm.

Two oral oncogenicity mice studies ([redacted] 1993a; [redacted] 1993b) were performed, since it became apparent after 6 months that the highest level of 3000 ppm would not meet the criteria for an MTD. Therefore the second study was initiated with dose levels up till 7000 ppm. The two studies evaluated together will fulfill the OECD 451.

In the **first mice study** ([redacted] 1993a) with dose of 0, 10, 100, 1000 and 3000 ppm fludioxonil mortality was unaffected by treatment with survival rates at 18 months of 74-86% and 71-92% for males and females respectively. Treatment-related clinical signs were limited to blue urine, dark faeces and blue staining of various areas of the body: findings are attributable to the excretion of the blue metabolite SYN 51852 and are not considered to be of toxicological significance.
Group mean bodyweights and weight gains were unaffected by treatment. For males statistically significantly increased food consumption was noted in the high dose from week 8-41 and higher water consumption at week 50-51. In females statistically significantly decreased food consumption was recorded only in the 100 ppm dose group at week 21.

The recorded ocular changes included corneal or lenticular opacity and pupil abnormality and were observed at comparable frequencies in control and high dose animals.

With respect to haematology no statistically significant differences were found for any parameter between control and any dose group males at 12 or 18-month.

Females in the high dose group has statistical significance increased absolute and relative liver weight after 18 month and statistical significance increase in the relative liver weight after 12 month. Significant increases in relative liver weight at the interim sacrifice were also seen in 10 ppm and 1000 ppm females, but are not considered to be related to treatment in the absence of a dose-response relationship; and the absence of similar findings at terminal sacrifice. A not significant increases in the relative liver weight (112% of control) were also seen for 3000 ppm males and could be of biological significance and potentially adverse. The effects on the liver weight at 3000 ppm is considered adverse.

Of non –neoplastic lesions blue staining of the skin and/or hair, urine discolouration, blue staining of the digestive or urogenital tract was seen at ≥1000 ppm in males and at 3000 ppm in females. These findings can be attributed to the presence of the blue-coloured metabolite SYN 518582 and are therefore not considered to be of toxicological significance.

Enlarged spleen was noted at slightly increased incidence in both sexes at 3000 ppm; no effect on spleen weigh or histopathological correlates were observed. High-dose females had slightly increased number

of enlarged thymus, liver and lymph nodes. No effect on thymus weight or histpathological correlates were observed to confirm the toxicological significance of the enlarged thymus.

There were generally high incidences of chronic inflammation of the lung (34-43/60 in males; 42-51/60 in females) and of the glandular mucosa of the stomach (34-48/60 in males; 27-37/60 in females) in all control and treated groups and in both sexes. Other changes recorded in this study were common findings in CD-1 mice at 18-month sacrifice.

A statistically significant increase in the incidence of lymphoma was seen in high dose females, the value is within the range of historical controls (13-32%; as the historical control data were presented in the original study report (conducted at [redacted])), eCA assumes that it was conducted within the same time period and same strain, the testing facilities were the same. However the time interval needs to be confirmed by the original data owner of the study which is the obligation of the applicant to provide). [redacted]. The incidence of lymphoma in females in the other dose groups were high but comparable to the incidence in control animals. Male mice had a lower incidence of lymphomas and did not show a similar increase as females did.
With respect to other neoplastic findings the tumour types as well as the incidences were normal in an 18-month CD-1 mouse study and were not reported with higher incidence in high-dose animals compared with control or other treated groups in either sex.

In the **second mice study** ([redacted] 1993b) with doses of 0, 3, 30, 5000 and 7000 ppm survival was markedly reduced in high dose animals with survival percentages at termination of 27% and 22% in males and females and associated with clinical signs including dyspnoea, hypothermia, pallor, hypoactivity, hunched posture and tremors. Increased mortality in this group became apparent from approximately one year and was mostly due to nephropathy. The top dose level therefore exceeds the maximum tolerated dose (MTD).
Additional clinical signs associated with the excretion of the blue metabolite SYN 518582 seen at dose levels of ≥5000 ppm are not considered to be adverse.
Statistical significance reduced weight gain by both sexes was apparent at ≥5000 ppm while bodyweights of 7000 ppm males were significantly lower than controls from Week 4, bodyweights of females at 5000 and 7000 ppm were significantly lower from Week 21. Food consumption was unaffected by treatment at any dose level, however slightly reduced food utilisation efficiency was seen in males at ≥5000 ppm.
Haematological investigations revealed changes in red blood cell parameters consistent with anaemia in both sexes at 7000 ppm in terms of reduced haemoglobin concentrations and haematocrit at 12 and 18 months and findings were associated with increased reticulocyte count. In addition, increased lymphocyte counts, reduced red blood cell counts, mean corpuscular haemoglobin and the relative counts of segmented neutrophils were observed in 7000 ppm females at 12 and/or 18 months.
Mean absolute and relative liver weights were increased in both sexes at ≥5000 ppm; findings were associated in both sexes with gross observations of discoloration of the liver and in males with discoloured foci.
Furthermore an increased incidence of hepatic cysts was also observed in males at 7000 ppm.
Histopathology revealed increased incidences of hepatocellular necrosis and bile duct hyperplasia in 7000 ppm males.
Statistical significance lower kidney weights (absolute) were seen in males at 7000 ppm, however values in females were elevated. The weight changes in the kidney were associated with general discoloration and cysts at 7000 ppm both sexes; discoloured foci and a rough pitted surface were additionally observed at ≥5000 ppm in both sexes. A dose-related increase in the incidence and severity of nephropathy was observed in both sexes at 5000 and 7000 ppm: findings were characterised by glomerular atrophy, hyaline change, tubular dilatation and protein cast formation, an irregular capsular outline due to fibrosis and thickening of the tubular basement membrane. There was also a marked

increase in the incidence of focal tubular calcification and a slightly increased severity of chronic inflammation at ≥5000 ppm.

There was no dose-related increase in the incidences of any specific neoplastic finding or with respect to total neoplasms at 5000 and 7000 ppm. This is in contrast to the high incidence of metastatic multicentric neoplasms and total neoplasms observed in female mice administered 3000 ppm. Furthermore, a statistically significantly increased incidence of lymphomas was also observed in 3000 ppm females but not in females at 5000 or 7000 ppm. It cannot be excluded that the marked reduced survival in females at 7000 ppm may have influenced the observed incidence of lymphomas at the 18-month terminal sacrifice; however, the incidence of lymphomas was similar in the 5000 ppm dose group and in the control group as was the survival (64 versus 71 % at 5000 ppm and in controls, respectively). As there is no clear dose response the increased incidences of lymphomas, metastatic multicentric neoplasms and total neoplasms in females administered 3000 ppm are not considered to be related to the treatment with fludioxonil although it cannot be clearly excluded.

Conclusion (study [redacted] 1993a and [redacted] 1993b):
Under the conditions of the two dietary carcinogenicity studies with Swiss mice of the CD-1 strain administered dietary concentrations of 0, 3, 10, 30, 100, 1000, 3000, 5000, or 7000 ppm fludioxonil technical for up to 18 months, the target organs were the liver, red blood cell and kidney.
Increased liver weights were observed from 3000 ppm in both sexes and bile duct hyperplasia in 7000 ppm males. In the kidneys nephropathy were observed in both sexes from 5000 ppm. Furthermore there were effects on the haematopoietic system as indicated by signs of anaemia in both sexes at 7000 ppm. The body weight and body weight gain were decreased from 5000 ppm and the survival was markedly reduced in animals at 7000 ppm. Thus 7000 ppm clearly exceeded the maximum tolerated dose (MTD) for fludioxonil and the data from this dose group should therefore be considered with reservation.
The NOAEL is considered to be 1000 ppm for both sexes corresponding to 112/133 mg/kg bw/day for males and females respectively based on the effects on the liver and the kidneys.

Fludioxonil is not carcinogenic in male or female mice at dietary doses up to 5000 ppm and probably also up to 7000 ppm.

No human data is available.

3.7.2 Long-term dermal toxicity

No data is available.

3.7.3 Long-term inhalation toxicity

No data is available.

3.7.4 Overall conclusion on long-term repeated dose toxicity

In rats administered dietary doses of up to 3000 ppm fludioxonil technical for up to 24 months effects were noted in both sexes at the highest dose level and included reduced body weight and body weight gain, signs of mild anaemia in females, gross necropsy and histopathological findings in the liver (both sexes) and the kidneys (males only). The NOAEL for chronic toxicity is considered to be 1000 ppm corresponding to 37 mg/kg bw/day in male rats and 44 mg/kg bw/day in female rats.
The incidences of hepatocellular adenomas and carcinomas were reported to be increased in all dose groups but within the ranges at the laboratory for the strain of rats. However, for male rats the incidences did not exhibit a dose-response relationship. For female rats the increased incidence in high-

dose females was not statistically significantly different from that in the control group and are well within the laboratory's historical control range. Therefore the hepatocellular tumours observed in this study are not considered to be related to the treatment with fludioxonil and thus fludioxonil is not considered to be carcinogenic in male or female rats at dietary doses up to 3000 ppm.

In mice administered dietary doses up to 7000 ppm fludioxonil technical for up to 18 months the survival was markedly reduced at 7000 ppm indicating that the substance was tested beyond the maximum tolerated dose (MTD) and the data from this dose group should therefore be considered with reservation. The body weight and body weight gain were decreased from 5000 ppm indicating that the MTD was achieved. Signs of anaemia were observed only at 7000 ppm. Increased liver weight was observed in both sexes from 3000 ppm; the only histopathological finding in the liver was bile duct hyperplasia in males at 7000 ppm. Nephropathy was identified in both sexes from 5000 ppm and was characterised by glomerular atrophy, hyaline change, tubular dilation, protein cast formation, an irregular capsular outline due to fibrosis, and tubular basement membrane thickening. There were also foci of mononuclear inflammatory cells and foci of tubular calcification, which were most numerous in the medulla.
The NOAEL for non-neoplastic findings is 1000 ppm corresponding to 112/133 mg/kg bw/day for males and females respectively.

The incidences of lymphomas, metastatic multicentric neoplasms and total neoplasms were high in female mice at 3000 ppm but were similar to the incidences in the control group at 5000 and 7000 ppm. It cannot be excluded that the marked reduced survival in females at 7000 ppm may have influenced the observed incidence of lymphomas at the 18-month terminal sacrifice. However, the incidence of lymphomas was similar in the 5000 ppm dose group and in the control group as was the survival (64 versus 71 % at 5000 ppm and in controls, respectively). As there is no clear dose response in the increased incidence of lymphomas, metastatic multicentric neoplasms and total neoplasms in females administered 3000 ppm is not considered to be related to the treatment with fludioxonil although it cannot be clearly excluded.
Fludioxonil is not considered to be carcinogenic in male or female mice at dietary doses up to 5000 ppm and probably also up to 7000 ppm.

Overall it is concluded that fludioxonil is not carcinogenic to rats and mice.

Classification:
No classification with respect to carcinogenicity or chronic effects is warranted for fludioxonil according to Regulation (EC) No 1272/2008.

3.8 GENOTOXICITY

3.8.1 In vitro

Summary table of *in vitro* genotoxicity studies						
Method, Guideline,GLP status, Reliability	**Test substance (purity%), Doses, End point**	**Relevant information about the study (e.g. cell type, strains)**	**Result**		**Remarks (e.g. major deviations)**	**Reference**
			without	**with**		
			metabolic activation			
Bacterial reverse mutation assay (OECD 471), GLP, 1	Fludioxonil ([redacted]) (20-5000 µg/plate) gene mutation	*S. typhimurium* TA 98, TA 100, TA 1535, TA 1537*;* *E. coli* WP2uvrA	negative	negative	-	Ogorek, B., 1989 (IUCLID 8.5.1-01)
In vitro mammalian cytogenetic test (OECD 473), GLP, 1	Fludioxonil ([redacted]) (3-350 µg/ml) cytogenetic: chromosome aberrations, polyploidy	Chinese hamster ovary (CHO) cells	positive	positive	Only 100 metaphases (instead of the 200 specified in the current OECD (1997 OECD guideline) were analysed).	Strasser, F.F., 1989 (IUCLID 8.5.2-01)
In vitro mammalian cell gene mutation test (OECD 476), GLP, 1	Fludioxonil ([redacted]) (0.5-60 µg/ml), gene mutation	Chinese hamster lung fibroblasts V79	negative	negative	-	Dollenmeier, P. 1989 (IUCLID 8.5.3-01)

Fludioxonil (CGA 173506) was tested at concentrations from 20 to 5000 µg/plate in Ames Salmonella/mammalian-microsome bacterial mutagenicity assay in S. Typhimurium TA98, TA100, TA1535, TA1537 and in E. Coli WPuvrA (OECD 471). In the mutagenicity tests the growth of the bacteria where occasionally inhibited at the upper concentrations. There was no indication of mutagenic activity in any of the bacterial strains employed in any of the tests. The array of positive control chemicals used in this assay induced significant increases in mutation frequencies and confirmed adequacy of the experimental conditions for detecting induced mutations.
No evidence for a mutagenic effect of fludioxonil was seen either in the absence or presence of a metabolic activation system under the experimental conditions used.

In the *in vitro* mammalian cytogenetic test (OECD 473) fludioxonil (CGA 173506) was tested at concentrations from 2.73 to 43.75 µg/mL without metabolic activation and 5.47 to 350 µg/mL with metabolic activation in a chromosome aberration test in Chinese hamster ovary cells. Marked cytotoxicity was seen at concentrations of ≥43.75 µg/ml. Appropriate positive control compounds confirmed the sensitivity of the assay in detecting structural and numerical chromosomal aberrations. Both with and without metabolic activation fludioxonil and/or it metabolites induced specific chromosome aberrations. The effect showed a concentration dependent tendency. Without metabolic activation the induction was seen at the highest concentration tested and with metabolic activation there was a statistical significant trend at the 3 highest concentrations. Fludioxonil also increased the number of polyploid cells which may indicate a potential to inhibit mitotic processes and to induce numerical chromosomal aberrations. Without metabolic activation and with 24 hours treatment the effect on the increased number of polyploid cells was clearly concentration dependent. It can therefore be concluded that under the experimental conditions used in this experiment fludioxonil showed a clastogenic potential *in vitro*.

In the *in vitro* mammalian cell gene mutation test (OECD 476) there was no evidence of mutagenicity under the conditions of this study, either in the absence or presence of metabolic activation. Slightly increased mutation frequencies were seen in one experiment in the absence of metabolic activation but were not reproducible and no relationship to the exposure concentration was apparent. The slight increase in mutation frequency (mutant factor 3.4) at the lowest concentration (1.0 µg/mL) without metabolic activation was observed in the confirmatory experiment. However, one of the acceptance criteria for a positive result is that the mutant frequency in a treated culture exceeds that of the negative control by a mutant factor of 3 and that the absolute number of clones in the treated and untreated culture differs by more than 20 clones per 106 cells. The difference between the mutation frequency of the sample and the mean mutation frequency of solvent controls was lower than 20×10^{-6}. Furthermore, no increase in mutation frequencies was observed at any other concentration of fludioxonil with or without metabolic activation in any of the experiments.

The test had a mutation frequency sensitivity limit of 4×10^{-6}. In all the experiments, at many concentrations of test substance as well as in negative controls, the mutation frequency was below this sensitivity limit. The mutant frequency of all these samples was set to 4×10^{-6} and the mutant factor therefore 1. Appropriate positive control compounds confirmed the sensitivity of the assay.

In conclusion fludioxonil was not mutagenic under the conditions of this study, either in the absence or presence of metabolic activation.

3.8.2 In vivo

Summary table of *in vivo* genotoxicity studies					
Method, Guideline,GLP status, Reliability	**Test substance (purity%), Doses, End point**	**Relevant information about the study (e.g. cell type, strains)**	**Result**	**Remarks (e.g. major deviations)**	**Reference**
Micronucleus test (OECD 474) GLP, 1	Fludioxonil ([redacted] (1250, 2500, 5000 mg/kg bw) chromosome aberrations (structural leading to micronuclei)	mouse bone marrow	negative	From OECD TG 474, 1997: only 1000 PCEs were evaluated. There was no sign of cytotoxicity in the bone marrow at the highest dose level tested.	[redacted] 1990 (IUCLID 8.6-01)
Chromosome aberration test (OECD 475) GLP, 1	Fludioxonil ([redacted] (1250, 2500, 5000 mg/kg bw) chromosome aberrations,	Chinese hamster bone marrow	negative	No information of cytotoxicity as the mitotic index was not determined	[redacted] 1993a (IUCLID 8.6-02)
UDS and replicative DNA synthesis test (OECD 486) GLP, 1	Fludioxonil [redacted] (2500, 5000 mg/kg bw), DNA damage	Rat hepatocytes	negative	-	[redacted] 1993b (IUCLID 8.6-03)

In the *in vivo* micronucleus test (OECD 474) there was no significant increase in the number of micronucleated PCE found in animals treated with fludioxonil.

There were no signs of cytotoxicity as the PCE/NCE ratio varied from 0.8 to 1.2 in all investigated animals. There was no sign of cytotoxicity in the bone marrow at the highest dose level tested confirming bone marrow exposure. However the ADME studies showed that fludioxonil administered orally (gavage) was quickly widely distributed in blood and various organs and tissues including the bone tissue. After 0.25 hr in the F1 and F3 dose groups 0.41% and 0.58% of the applied dose was found in bone tissue in male and females respectively. An initial Cmax was apparent at 15 minutes after oral administration of a low dose of 0.5 mg/kg bw, with a second smaller peak seen at 12 hours showing rapid distribution and within the time frame of the micronucleus study. Given the presence of the active substance in the blood and detection in bone tissue together with a high oral absorption and no evidence of bioaccumulation, a good potential for exposure to the target cells in the bone marrow is predicted, as this tissue has a good blood supply.

The positive control chemical used in the test induced significant increases in the number of micronucleated PCE and confirmed adequacy of the experimental conditions for detecting induction of

micronuclei.
In conclusion fludioxonil did not show a clastogenic potential *in vivo* under the conditions of this study.

In the *in vivo* chromosome aberration test (OECD 475) there was no statistically significant increase in the number of metaphases containing specific chromosome aberrations in the animals treated with fludioxonil compared to control animals. Furthermore, there was no significant difference in the incidence of polyploid metaphases in the animals treated with fludioxonil compared to the negative control.
There are no measurements of cytotoxicity in the bone marrow as e.g. the mitotic index in the bone marrow. The doses used in the experiment were high. However the ADME studies showed that fludioxonil administered orally (gavage) was quickly widely distributed in blood and various organs and tissues including the bone tissue. After 0.25 hr in the F1 and F3 dose groups 0.41% and 0.58 % of the applied dose was found in bone tissue in male and females respectively. An initial Cmax was apparent at 15 minutes after oral administration of a low dose of 0.5 mg/kg bw, with a second smaller peak seen at 12 hours showing rapid distribution. Given the presence of the active substance in the blood and detection in bone tissue together with a high oral absorption and no evidence of bioaccumulation, a good potential for exposure to the target cells in the bone marrow is predicted, as taken into consideration that this tissue has a good blood supply.
The positive control compound induced significant increases in the proportion of aberrations, confirming the sensitivity of the assay.
In conclusion fludioxonil did not show a clastogenic potential or spindle toxicity *in vivo* under the particular conditions used in the experiment.

In the *in vivo*/*in vitro* unscheduled and replicative DNA synthesis in rat hepatocytes (OECD 486), there were no differences in either gross or nett nuclear grains in the hepatocytes from fludioxonil treated animals compared to the negative control. The percentage distribution of the nuclear grain counts revealed no differences either.
Positive control compounds demonstrated the sensitivity of the assay to detect UDS and replicative DNA synthesis.
In conclusion there was no evidence of unscheduled DNA synthesis (UDS) in hepatocytes as indication of DNA repair succeeding DNA damage after treatment with fludioxonil under the condition of this study.

No human data is available.

Fludioxonil was not shown to be genotoxic *in vivo* in somatic cells therefore testing for genotoxicity *in vivo* in germ cells is not required.

3.8.3 Overall conclusion on genotoxicity

***In vitro*:**
Fludioxonil, CGA 173506 did not show mutagenic potential *in vitro* studies on different strains of bacteria cells or mammalian cells (hamster). The substance showed a clastogenic potential in Chinese Hamster ovary cells where specific chromosome aberrations were induced both with and without metabolic activation. The effect showed a concentration dependent tendency. Fludioxonil also increased the number of polyploid cells which may indicate a potential to inhibit mitotic processes and to induce numerical chromosomal aberrations.

***In vivo*:**
In the three *in vivo* tests counting a micronucleus test on mouse bone marrow, chromosome aberration test on hamster bone marrow and a UDS test on rat hepatocytes no positive results were obtained.

The substance did not show a clastogenic potential in the bone marrow of the Chinese hamster, in the bone marrow of the mouse and no indication of DNA repair as result of DNA damage were observed in the rat hepatocytes.

On the basis of the submitted tests it is concluded that overall the substance did not show a genotoxic potential.
Fludioxonil did show a clastogenic potential *in vitro* but not in vivo. On the basis of the present tests no classification with respect to genotoxicity is warranted according to Regulation (EC) No 1272/2008.

3.9 CARCINOGENICITY

Evaluated under 3.7.1 long-term repeated dose toxicity (combined chronic and carcinogenicity studies).

3.10 REPRODUCTIVE TOXICITY

3.10.1 Developmental toxicity

	Summary table of animal studies on adverse effects on development						
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/ group**	**Test substance Dose levels, Duration of exposure**	**NOAEL (mg/kg bw/day)** Maternal/ developmental	**LOAEL (mg/kg bw/day)** Maternal/ developmental	**Results/critical effects**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 414 GLP, 1	Rat Sprague Dawley 25 mated females /group	Fludioxonil ([redacted]) 0, 10, 100 or 1000 mg/kg bw day	100 / 1000	1000 / -	Dams: Reduced body weight gain and food consumption at 1000 mg/kg bw/day. Foetuses: No effects.	17 instead of 20 pregnant females at low dose	[redacted] 1989a (IUCLID 8.10.1-01)
OECD 414 GLP, 1	Rabbit NZW 16 inseminated females /group	Fludioxonil [redacted] 0, 10, 100 or 300 mg/kg bw day	100 / 300	300 / -	Dams: Reduced body weight gain and food consumption at 300 mg/kg bw/day. Foetuses: No effects.		[redacted] 1989b (IUCLID 8.10.1-02)

Two developmental toxicity studies performed in rats and in rabbits are available for evaluation.

In the developmental toxicity study performed according to OECD 414 administration by gavage of 97.5% pure fludioxonil to pregnant Sprague-Dawley rats at daily doses of 0, 10, 100, or 1000 mg/kg bw on days 6 through 15 of gestation resulted in maternal toxicity in the form of reduced food consumption (10% compared to control) and mean bodyweight gain (21% compared to control) on days 6-11 in the high dose. Statistical significant reduced weight gain by animals at 1000 mg/kg bw/d during the dosing phase resulted in significantly reduced corrected weight gain over the study period (day 0-20). Gravid uterus weights were unaffected by treatment. No treatment-related mortality occurred and no signs of toxicity were observed during the study period. Macroscopic examination revealed one female with a pale liver.
No treatment-related effects were noted on the numbers of implantation sites, pre-implantation loss, early or late resorptions in any group. Total resorption was seen in two females at 10 and 100 mg/kg bw/d, these animals had few (1-3) implantation sites and the rate of resorption was not statistical significantly different from control group and are not considered to be treatment-related. There were no dead foetuses in any group. The numbers of live foetuses per litter, foetal sex ratio and foetal weights were not significantly different from control and did not show any dose-relationship.

No toxicological relevance is attributed to the significantly lower incidences of skeletal variations and anomalies observed in the treated groups; findings are considered to represent normal biological variation.
The incidence of foetuses with dilatation of the ureter and/or renal pelvis was slightly (but not significantly) increased at 1000 mg/kg bw/d compared to controls. This finding is considered to be incidental as the foetal incidences in this group (4.0% and 5.6% respectively) are within the laboratory's historical control range of 0.6-7.5%. The validity of the historical control data has not been confirmed with respect to strain, time interval and laboratory. [redacted]
It is additionally noted that the concurrent control incidences for these findings are at the lower end of the laboratory's historical range.

Conclusion:
Based on the effect on maternal toxicity (reduced body weight gain and food consumption) in the high-dose group a NOAEL for maternal toxicity is set to 100 mg/kg bw/day. The incidence of litters having foetuses with foetal soft tissue abnormalities (ureteral and/or pelvic dilations) is considered to be incidental and within the HCD of the laboratory and not considered to be treatment related. The NOAEL for developmental toxicity is set to 1000 mg/kg bw/day.

In the second developmental toxicity study pregnant NZW rabbits ([redacted]. 1989b) were given daily doses of 0, 10, 100 or 300 mg/kg bw/day on day 6 through 18 of gestation which resulted in maternal toxicity in form of reduced body weight gain at the two highest doses (100 and 300 mg/kg bw/day) and food consumption in the high dose only.

At 100 mg/kg bw/day the reduction was less pronounced at not accompanied with a marked reduction in food consumption as at the top dose level. The reduction in body weight gain was 17% lower during dosing period day 6-18 compared to the concurrent control, this was not accompanying with a reduction in food consumption as in the high dose. Applicant argued that the finding was not clearly related to treatment due to the magnitude of change and that bodyweight values for individual animals in this group are within the concurrent control range and mean values are within the laboratory's historical control range (further details of bodyweight gain data is tabulated in the applicant´s discussion paper for ad hoc follow-up ; to be included in IUCLID under this study) . Additional consideration was based on the fact that body weight gain in pregnant rabbits may not be useful indicators of maternal toxicity because of normal flucation in body weight gain during pregnancy (Guidance on the Applicaton of CLP Criteria, 2015). In light of the statement in the Guidance on the Applicaton of CLP Criteria, 2015 regarding pregnant rabbit and normal fluctuation in bw gain changes it could also be considered whether it is more appropriate to compare with the HCD data.

In the high dose group the food consumption of pregnant rabbits was statistically significantly decreased on days 6-12 and remained lower than that of the control group during the rest of the study. The mean body weight gain of pregnant rabbits was decreased by 50 % during the dosing period compared to control.

The majority of the Ad-hoc follow up group supported to raise the NOAEL for maternal toxicity from 10 to 100 mg/kg bw/day.

The gravid uterine weight was comparable between the control and all dose groups.

No treatment-related mortality occurred and no treatment-related effects on pregnancy status were observed. Treatment-related clinical signs were limited to blue urine in animals at 100 and 300 mg/kg bw/d; this finding is due to the excretion of a blue metabolite and is not considered to be of toxicological significance.

No treatment-related effects were noted on the mean numbers of implantation sites, pre-implantation loss, early and late resorptions and on the incidences of external, skeletal or visceral abnormalities Foetal weight was comparable in all groups. A marginal difference (however statistically significant) in the sex ratio of foetuses at 300 mg/kg bw/day were observed; the toxicological significance is unclear but is expected not to be related to treatment since the critical time of sexual differentiation is after birth and gender is primarily determined at fertilization by the genetic setup of the zygote Therefore the changes in sex ratio (more females 52% versus 48% males) is considered incidental. No differences in sex ratios were observed in the developmental rat study or in the two-generation study.

Conclusion:
Based on effect on maternal toxicity (reduced body weight gain) in the two high dose groups the NOAEL for maternal toxicity is set to 100 mg/kg bw/day based on more pronounced effects on the bw gain and food consumption at the top dose of 300 mg/kg bw/day..
The NOAEL for developmental toxicity is 300 mg/kg bw/day due to no treatment related foetotoxic effects at the highest dose.

No human data are available.

3.10.2 Fertility

	Summary table of animal studies on adverse effects on fertility						
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/ group**	**Test substance Dose levels, Duration of exposure**	**NOAEL (mg/kg bw/day)** Parental (overall) / offspring/reproduction	**LOAEL (mg/kg bw/day)** Parental (overall) / offspring/reproduction	**Results/critical effects**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 416 GLP, 1	Rat Sprague Dawley	Fludioxonil [redacted] 0, 30, 300, or 3000 ppm (equal to an average of 0, 2.1, 21, or 212 mg/kg bw/day)	21 /21/ 212	212 / 212/-	Decreased body weight and body weight gain of parental rats and pups at 212 mg/kg bw/day. No reproductive effects.	-	[redacted], 1992 (IUCLID 8.10.2-01)

In the two-generation study (one litter per generation) in Sprague-Dawley rats performed according to OECD TG 416, males and females were fed 95.4% pure fludioxonil at dietary doses of 0, 30, 300 and 3000 ppm (equivalent to ~0, 2.1, 21 or 212 mg/kg bw/day) continuously throughout a 10 week pre-mating period, mating, gestation and lactation of the resulting F1 offspring. Litters were reduced to eight pups (4/sex where possible) at Day 4 post partum. Exposure of selected F1 pups was continued following weaning for a 12-week pre-mating period and throughout mating, gestation and lactation of the resulting F2 offspring.

There were no treatment-related mortalities in either of the parental generations. Discolouration of the penis/scrotum in males and perineum in females at 3000 ppm is attributable to the excretion of the blue-coloured metabolite SYN 518582 and is not considered to be of toxicological relevance.
At the highest dose level of 3000 ppm fludioxonil caused treatment-related effects in the parental animals as well as in the pups.
Statistical significant reduced mean bodyweight in F1 males and F0 females (premating, gestation and lactation) correlated well with a statistical significant reduced food consumption in F1 males and F0 females. Furthermore cumulative bodyweight gain was statistical significantly reduced in F0 females during premating and lactation at 3000 ppm.

A marginal increase (statistical significant) in relative testes weight in F1 males at 3000 ppm and a marginal reduction in absolute ovary weight in F0 females at 3000 ppm are considered to be secondary to the lower terminal bodyweights in these animals. In the absence of a dose-response relationship, the marginal reduction in absolute ovary weight seen in F0 females at 30 ppm is considered to be without toxicological significance.
Also at the high dose group of 3000 ppm statistically significant reductions in mean F1 and F2 pup body weight were observed in both sexes.
The numbers of implantation sites and litter sizes were slightly higher at 300 and 3000 ppm in the F2 generation, but are considered to be within the normal biological variation and therefore unrelated to treatment. A marginally higher number of pups from these litters died within the first 4 days post partum, however findings are attributable to the larger litter sizes in these groups and are therefore also considered to be unrelated to treatment. There were no clinical signs that were attributable to treatment.
Fludioxonil did not alter the reproductive performance or caused any other organ weight (than those mentioned before), gross or histopathological changes of the examined organs (mainly reproductive).
Fludioxonil did not alter the litter parameters either, or caused gross changes in the pups.
No treatment related effects were observed at the lower doses.

Conclusion:
Reduced bodyweight and body weight gain were observed at the highest dose level in parental animals and offspring. Additionally, food consumption was occasionally decreased in parental animals at 3000 ppm. All reproductive and litter parameters were unaffected by treatment; treatment-related findings in offspring were limited to reduced weight at 3000 ppm.
A reproductive overall NOAEL of 3000 ppm (equivalent to 212 mg/kg bw day) was determined based on no treatment-related effects on reproductive parameters at the top dose level.

An overall NOAEL for parental and pup toxicity of 300 ppm (equivalent to 21 mg/kg bw/day) can be determined, based on the bodyweight effects in both sexes at 3000 ppm (equivalent to 212 mg/kg bw day).

No human data is available.

3.10.3 Effects on or via lactation

No specific effect on lactation was observed in the 2 -generation rat study.

3.10.4 Overall conclusion on reproductive toxicity

Fludioxonil was not toxic to reproduction in the two-generation study in rats at daily dietary doses up to 212 mg/kg bw/day, a dose level at which parental toxicity was observed. In the developmental toxicity studies in rats and rabbits, no treatment-related effects on the foetuses were observed at any dose level even though maternal toxicity occurred at the high dose levels (1000 mg/kg bw/day in rats, 100 mg/kg bw/day in rabbits).

Classification:
No classification with respect to fertility or developmental toxicity is warranted for fludioxonil according to Regulation (EC) No 1272/2008.

3.11 NEUROTOXICITY

No data were submitted. Fludioxonil has no structural relationship to neurotoxic substances. Moreover no evidence of neurotoxic potential are seen in the toxicological studies. No specific studies are required.

3.12 IMMUNOTOXICITY

No evidence of immunotoxicity was seen in any of the standard toxicity studies performed with fludioxonil. The structure and mechanism of action of fludioxonil do not raise any concerns of relevance to immunotoxicity.
Specific studies of immunotoxicity are not required.

3.13 DISRUPTION OF THE ENDOCRINE SYSTEM

Please refer to section 4.3 Endocrine disrupting properties.

3.14 FURTHER HUMAN DATA

The routine surveillance of plant personnel involved in the manufacture and formulation of fludioxonil has not revealed any health effects attributable to exposure to fludioxonil. No poisoning cases have been reported to the company and no cases are reported in the scientific literature. No epidemiological studies relating to fludioxonil exposure are reported in the literature.

For more specific medical surveillance data on manufacturing plant personnel please refer to the confidential information in Appendix VI.

3.15 OTHER DATA

No data is available.

4 ENVIRONMENTAL EFFECTS ASSESSMENT

All the environmental data requirements for product-type 7 (film preservatives), 9 (fibre, leather, rubber and polymerised materials preservatives) and 10 (construction material preservatives) were addressed by studies.
The batches used in the key environmental studies covers the current technical specification and therefore the environmental assessment of fludioxonil. Please refer to Annex VI in this CAR to document "Evaluation of the representativeness of the technical specification of fludioxonil in the batches used in the environmenatl studies" prepared for the Ad hoc follow up WG_IV 2016 for fludioxonil batches.

4.1 FATE AND DISTRIBUTION IN THE ENVIRONMENT

4.1.1 Degradation

4.1.1.1 Abiotic degradation

Hydrolysis
The abiotic degradation of fludioxonil in the dark (i.e. hydrolysis) was investigated in one study at 25 °C in sterile aqueous buffer solutions at pH values of 5, 7 and 9 following the test of US EPA Pesticide Assessment Guidelines, subdivision N, paragraph 161-1. The test vessels with test substance were incubated in the dark for up to 30 days. No degradation was measured (radioactivity) during the 30 days, therefore fludioxonil is considered to be hydrolytically stable.
For the breakdown product CGA 339833 hydrolysis was investigated in a preliminary test conducted at pH values of 4, 7 and 9 at 50 °C and in a main test at pH 7 and 9 at 50, 61 and 75 °C following OECD 111. The results show that CGA 339833 is more rapidly hydrolysed at pH 9 than at pH 7 and 4. The degradation followed first order kinetics. At pH 7 the extrapolated DT50 of 597 days at 25 °C (calculated by Arrhenius equation) reveals that at usually occurring environmental temperatures the hydrolysis will be very slow.

Summary table - Hydrolysis							
Method, Guideline, GLP status, Realibility	**pH**	**Temp. [°C]**	**Initial TS concentration, C_0[mg/L]**	**Half-life, DT_{50} [d]**	**Coefficient of correlation, r^2**	**Remarks**	**Reference**
Fludioxonil							
US EPA subdivision N, para. 161-1, following GLP, 1	5, 7, 9	25	1	Not available	Not available		Hawkins, D.R. et al., 1991a (IUCLID 10.1.1.1-01)
CGA 339833							
OECD 111, following GLP, 1	7, 9	50, 61, 75	1.2 at all pH's and temperatures	597 (calculated for pH 7 and 25 °C)	Not available	Test of CGA 339833 preliminary test performed at pH 4, 7 and 9 and 50 °C	Van der Gaauw, A., 2002 (IUCLUD 10.1.1.1-02)

Value used in Risk Assessment	
Value/conclusion	Hydrolysis of fludioxonil is not relevant
Justification for the value/conclusion	Fludioxonil is stable to hydrolysis at environmental relevant pH values at a temperature of 25 °C

Phototransformation in water

Fludioxonil is quickly degraded by photolysis in sterile aqueous solution, with a first order half-life equivalent to ca 10 days of natural sunlight at latitude 30°N and ca 9 days of natural sunlight at latitude 40°N, assuming 12 hours of daylight (IUCLID 10.1.1.1-03 and 10.1.1.1-04). In addition to CO_2 (5% and 20% AR with pyrrole and phenyl label, respectively) a number of minor photo-products (for example CGA 308565 at 6-7% AR) and three major photo-products were found in increasing concentrations until the end of the incubation period (Day 30). These major photo-degradation products were further investigated in separate studies (IUCLID 10.1.1.1-05/06) and were identified as CGA 339833 (max. 30.5% AR), CGA 344623 (max. 12.4% AR) and A5 at 11.5% AR.

Summary table – Photolysis in water							
Method, Guideline, GLP status, Realibility	**Initial molar TS concentra-tion [mg/L]**	**Total recovery of test substance [% of appl. AS]**	**Photolysis rate constant (k^c_p) [d^{-1}]**	**Reaction quantum yield ($\varphi^c E$)**	**Half-life ($t_{1/2E}$) [d]**	**Remarks**	**Reference**
US EPA subdivision N, para. 161-2, following GLP, 2	1	92.4-99.3 (from raw data)	0.0699	2.6 x 10^{-3} mol $Einstein^{-1}$ Latitude 30°N	9.9 days at 25 °C	[pyrrole-^{14}C]-fludioxonil was tested	Kirkpatrick, D., 1994a (IUCLID 10.1.1.1-03)
US EPA subdivision N, para. 161-2, following GLP, 2	0.51	91.8-99.5 (from raw data)	0.0795	2.6 x 10^{-3} mol $Einstein^{-1}$ Latitude 40°N	8.7 days at 25 °C	[phenyl-^{14}C]-fludioxonil was tested	Kirkpatrick, D., 1994b (IUCLID 10.1.1.1-04)

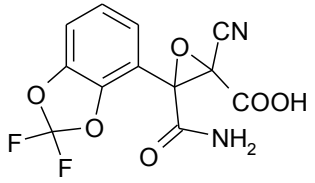
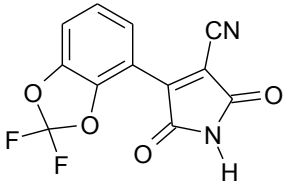
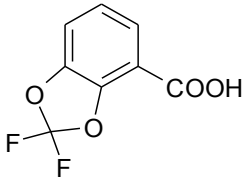
Value used in Risk Assessment	
Value/conclusion	9.9 days at 25 °C (28 days at 12 °C by using Arrhenius equation)
Justification for the value/conclusion	The highest value is chosen

Phototransformation in soil

Photolysis represents a major pathway of degradation for fludioxonil and the degradation rate for fludioxonil in light-exposed soil and the formation of photo-degradation products were calculated in three studies conducted at 25°C (Kirkpatrick, D., 1994d, e and f, IUCLID 10.2.1-14 to IIIA 10.2.1-16).

In thin layer soil plates (1 mm) in the laboratory, fludioxonil degraded with half-lives of 10 and 9 days equivalent of natural sunlight, these values are calculated using first order degradation kinetics.

The major soil photolysis products were CGA 339833 (9.1% AR), CGA 192155 (11.7%) and CGA 265378 (12.3%) which reached maximum levels after ca 19 days of natural sunlight.

CGA 339833	CGA 265378	CGA 192155
		

Summary table – Photolysis in soil					
Method, Guideline, GLP status, Realibility	**Soil**	**Total recovery of test substance [% of appl. AS]**	**Half-life ($t_{1/2E}$) [d]**	**Remarks**	**Reference**
US EPA subdivision N, para. 161-3, following GLP, 2	Sandy loam soil from Somersham, Cambridge, UK, 1 mm thickness, pH 6.5, 4.1 % org. C, 5 kg a.s./ha (0.05 mg/cm^2), 25 °C	95.7-96.5% (irridated soil after 7 days, i.e. 44 days of natural sunlight at lat. 30 °N), 99.6-101.5% (dark control soil after 7 days)	10 days at 25 °C (28 days at 12 °C)	[pyrrole-^{14}C]-fludioxonil was tested. 11.7% CGA 192155, 9.1% CGA 339833 and 12.3% CGA 265378 were formed	Kirkpatrick, D., 1994d and 1994f (IUCLID 10.2.1-14 and 10.2.1-16)
US EPA subdivision N, para. 161-2, following GLP, 2	Sandy loam soil from Somersham, Cambridge, UK, 1 mm thickness, pH 7, 3 % org. C, 5 kg a.s./ha (0.05 mg/cm^2), 25 °C	94.7-96.9% (irridated soil after 30 days, i.e. 44 days of natural sunlight at lat. 40 °N), 98.6-98.7% (dark control soil after 30 days)	9 days at 25 °C (25 days at 12 °C)	[phenyl-^{14}C]-fludioxonil was tested. 10% CGA 192155, 6% CGA 339833 and 2% CGA 265378 were formed	Kirkpatrick, D., 1994e (IUCLID 10.2.1-15)

Value used in Risk Assessment	
Value/conclusion	Half-life of 10 days at 25 °C (28 days at 12 °C by using Arrhenius equation)
Justification for the value/conclusion	The highest value is chosen

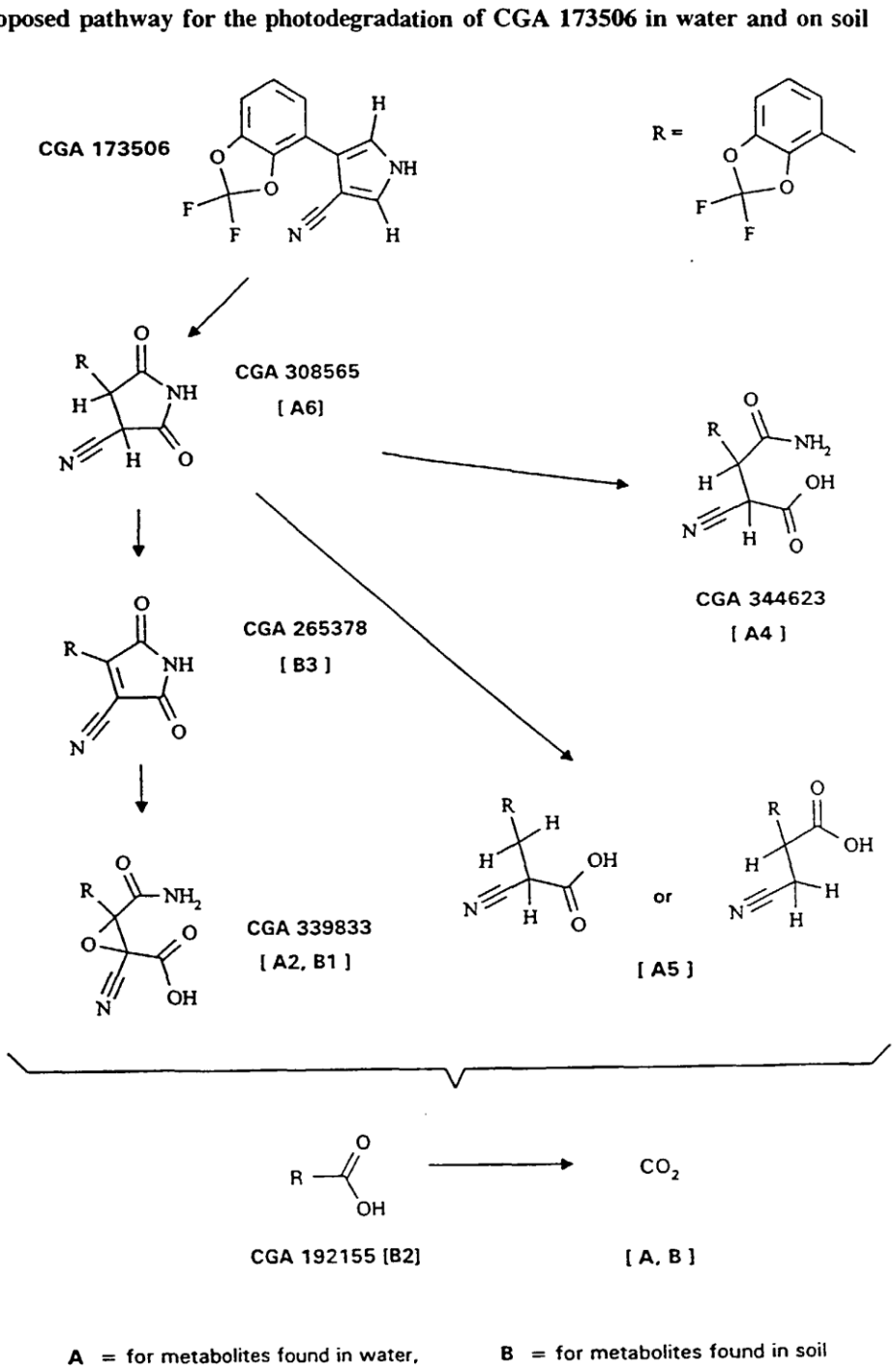


Figure 4.1-1: Proposed photo-degradation pathway for fludioxonil in water and on soil

The photo transformation products are described further in section 4.1.5.

Estimated photo-oxidation in air

Fludioxonil has a low vapour pressure of 3.9 x 10^{-7} Pa (at 25ºC) and a low Henry's law constant of ca. 5.4 x 10^{-5} m^3 Pa mol^{-1}. Therefore, volatilisation from soil or water is not expected to be a significant entry route into air for fludioxonil. Based on Atkinson calculation (Stamm, 1999; IUCLID 10.3.1-01), standard conditions, 5 x 10^5 OH radicals/cm^3, 24 hour day, the photochemical oxidative degradation in air would proceed with a half-live of 6.7 hours (3.6 hours for a 12 hour day, 1.5 x 10^6 OH radicals/cm^3). Overall, it is not expected that fludioxonil would be present in air for extended time periods or be transported over long distances or into the stratosphere.

Summary table – Photo-oxidation in air					
Model	**Light protection (yes/no)**	**Estimated daily (24h) OH concentration [OH/cm³]**	**Overall OH rate constant [cm³/molecule ec]**	**Half-life [hr]**	**Reference**
AOPWIN	no	5 x 10^5	57.6 x 10^{-12}	6.69	Stamm, E., 1992 (IUCLID 10.3.1-01)

Value used in Risk Assessment	
Value/conclusion	Half-live of 6.7 hours (24 hour day, 5 x 10^5 OH radicals/cm^3)
Justification for the value/conclusion	Estimated value from AOPWIN

4.1.1.2 Biotic degradation

4.1.1.2.1 Biodegradability (ready/inherent)

Fludioxonil is not classified as readily biodegradable according to the results of a CO_2 evolution test (IUCLID 10.1.1.2-01). Inherent biodegradability test is not performed as degradation in water/sediment and soil systems exist.

Summary table - biodegradation studies (ready/inherent)											
Method, Guideline, GLP status, Realibility	**Test type[1]**	**Test parameter**	**Inoculum**			**Additional substrate**	**Test sub-stance concentr. [mg/L]**	**Degradation**		**Remarks**	**Reference**
			Type	Concen tration	Adap-tation			Incuba-tion period	Degree [%]		
EC methods C.4-C, following GLP, 2	Ready	CO_2	Activa ted sludg e	Not stated	No	No	27.6 and 26.7	29 days	7	None	Baumann, W., 1993 (IUCLID 10.1.1.2-01)

Value used in Risk Assessment	
Value/conclusion	Not readily biodegradable
Justification for the value/conclusion	Only 7% of the substance is degraded within the incubation period

4.1.1.3 Rate and route of degradation including indentification of metabolites and degradation products

4.1.1.3.1 Biological sewage treatment

No degradation study in sewage treatment plant exist.

4.1.1.3.2 Biodegradation in freshwater

The distribution, degradation and metabolism of ^{14}C-labelled fludioxonil was investigated in equilibrated water-sediment systems.

Water/sediment degradation test

In a study conducted in the dark at 20°C (Gonzalez-Valero, 1992; IUCLID 10.1.3-01), fludioxonil rapidly dissipated from the water phase in two laboratory water/sediment systems (DT50 water = 1-2 days) due to adsorption to the sediment (max 94.5% AR at Day 30). Degradation in the whole system was slow, with a first order DT50 total system = 451-699 days (855-1326 days at 12 °C, Arhenius equation). Minor metabolites were formed in the sediment and water, accounting for 0.1 to 5% AR in the sediment and water, these were not identified. Mineralisation to CO_2 accounted for less than 2% AR.

Summary table – fresh water/sediment degradation

Method, Guideline, GLP status, Reliability	Test type[2]	Exposure	Test system		Test substance concentration	Incubation period	Degradation (DT_{50})	Remarks	Reference
			Water	Sediment					
US EPA subdivision N, para. 162-4[1], following GLP, 2	according to OECD 308	Aerated, dark, 20 °C	Pond (near Tugbach, CH), layer of 3,5-4 cm	Pond (near Tugbach, CH), silt/clay layer of 2-2.5 cm	~300µg/L	177 days	Whole system 699 d First order kinetics	Formation of five minor metabolites (6.3%) was observed, but not identified further	Gonzalez-Valero, J., 1992 (IUCLID 10.1.3-01)
			River (Rhine), layer of 3,5-4 cm	River (Rhine), sandy layer of 2-2.5 cm			Whole system 451 d First order kinetics		

[1] Also guidelines for the official testing of plant protection products, part IV, 5-1, German BBA and Dutch registration guideline, Section G.2.2 are used.

[2] Test according to OECD criteria

Value used in Risk Assessment	
Value/conclusion	699 days at 20℃, 1326 days at 12 ℃
Justification for the value/conclusion	The highest value is chosen as less than three values are available

4.1.1.3.3 Biodegradation in seawater

Data waiving	
Information requirement	No study on biodegradation in seawater is submitted
[redacted]	[redacted]

4.1.1.3.4 Biodegradation during manue storage

Data waiving	
Information requirement	No study on biodegradation in manure is submitted
Justification	[redacted]

4.1.1.3.5 Biotic degradation in soil

4.1.1.3.5.1 Laboratory soil degradation studies

Aerobic biodegradation

Eight aerobic laboratory soil degradation studies were performed in the dark with both [14C]-pyrrole and [U-14C]-phenyl labelled fludioxonil (IUCLID 10.2.1-01 to 10.2.1-08). Nine different soils were incubated under various conditions with respect to temperature (10ºC, 20ºC, 25ºC and 30ºC), moisture (30%, 60% and 75% of FC or 40% MWHC), and initial concentration of fludioxonil (0.048 – 11 mg/kg soil), with incubation periods

between 84 days and 1 year. Fludioxonil was slightly degradable in soil, with CO_2 (0.6 - 11.1% AR (pyrrole labelled) and 10.8 - 20.5% AR (phenyl-labelled) after 90 days at 20ºC) and bound residues (2.4 - 18.0% AR (pyrrole-labelled) and 17.3 - 19.4% AR (phenyl-labelled) after 90 days at 20ºC) observed as the principal degradates in all studies. Soil metabolites of fludioxonil were observed only in small amounts (total 0.3-8.4% AR).

The rate of degradation of fludioxonil in soil under dark aerobic conditions was investigated in the same studies employed to investigate the route of degradation. Test substance concentrations of 2 mg/kg and higher were not accepted due to possible effects on soil microorganisms as effects were found at this concentration level. This procedure was however not followed in the pesticide evaluation performed in 2007. The degradation of fludioxonil was considered using biphasic kinetics and degradation rates were calculated in most cases by a "best fit" function using a two compartment first order model, resulting in estimated experimental DT50 values in the range of 143 days to 482 days (geomean of 265 days, n= 8, 20 °C). When recalculated to 12 °C using the Arrhenius equation a DT50 of 502 days is achieved.

For the photo degradation product CGA 192155 experimental DT50 values ranged from 16 to 24 days in three soils at 20 °C, when recalculating the highest value of 24 days to 12 °C using the Arrhenius equation a DT50 of 46 days is achieved.

For the photo degradation product CGA 339833 experimental DT50 values ranged from 9.3 to 16 days in three soils at 20 °C, when recalculating the highest value of 16 days to 12 °C using the Arrhenius equation a DT50 of 30 days is achieved.

Summary table – aerobic biodegradation in soil- laboratory study											
Method, Guideline, GLP status, Reliability	**Test type[1]**	**Exposure**	**Test system**				**Test substance concentration**	**Incubation period**	**Degradation DT_{50}**	**Remarks**	**Reference**
			Soil origin	Soil type	pH	OC %					
US EPA subdivision N, para. 162-1 and 162-2[2], following GLP, 3	Aerobic and aerobic/anaerobic primary degradation (compared to OECD 304 and 307)	Dark, 25 °C, moisture level of 75% FC	Goole Humberside, UK	Sandy silt loam	7.9	4.8% OM	10-11 mg/kg corresponding to a field use rate of 7.5-8.25 kg/ha	365 d (aerobic), 90 d (aerobic/anaerobic)	>365 days	[pyrrole-^{14}C]-fludioxonil was tested. No major metabolites (10% AR) were identified	Hawkins, D.R. et al., 1999b (IUCLID 10.2.1-01)
			Somersham Cambri	Sandy loam	6.5	4.1% OM					

			dgeshire, UK								
Dutch registration guidelines, Jan 1987, section G 1, Section 6.2.C, following GLP, 2	Aerobic primary degradation (compared to OECD 304 and 307)	Dark, 20 and 10 °C, and two moisture levels (30 and 60% FC)	Les Evouettes	Sandy loam	5.4	1.8	0.2 and 2 mg/kg corresponding to a field rate of 150 and 1500 g a.i./ha	362 d	>365 days (482 days for 0.2 mg/kg)	[pyrrole-^{14}C]-fludioxonil was tested. Two metabolites observed maximum 7.1% of fraction 1 and 6.6% of fraction 2	Abildt, U., 1991 (IUCLID 10.2.1-02)
Richtlinie für die amtliche Prüfung von Pflanzenschutzmitteln, Teil IV, 4-1. Biologische Bundesanstalt für Land- und Forstwirtschaft, Germany, December 1986., following GLP, 3	Aerobic primary degradation (compared to OECD 304 and 307)	Dark, 20 °C and moisture level of 40% MWC (58% FC in Stein and 93% FC in Neuhofen)	Stein (10/90)	Sandy loam	7.0	1.3	2 mg/kg corresponding to a field rate of 1500 g a.i./ha	181 d	>181 days	[pyrrole-^{14}C]-fludioxonil was tested. Six metabolites observed (<9%)	Ellgehausen, H., 1992a (IUCLID 10.2.1-03)
			Neuhofen (SP 229)	Sandy	6.6	2.0					
No guideline cited, following GLP, 3	Aerobic primary degradation (compared to OECD 304 and 307)	Dark, 20 and 30 °C and moisture level of 40% MWC	Stein	Sandy loam	7.0	1.3	0.2 mg/kg corresponding to a field rate of 150 g a.i./ha	84 d	>84 d (20 °C) and 79 days (30 °C)	[pyrrole-^{14}C]-fludioxonil was tested. Two metabolites observed	Ellgehausen, H., 1992b (IUCLID 10.2.1-04)

										(<3%)	
Richtlinie für die amtliche Prüfung von Pflanzenschutzmitteln, Teil IV, 4-1. Biologische Bundesanstalt für Land- und Forstwirtschaft, Germany, December 1986., following GLP, 2	Aerobic and aerobic/anaerobic primary degradation (compared to OECD 304 and 307)	Dark, 20 °C and moisture level of 40% MWC (56% FC)	Stein	Sandy loam	7.0	1.3	0.2 mg/kg corresponding to a field rate of 150 g a.i./ha	364 d (aerobic) 90 d (anaerobic)	Aerobic: 313 days Aerobic/anaerobic: >90 days	[pyrrole-^{14}C]-fludioxonil was tested. Two metabolites observed (<3%)	Minet, U., 1994a (IUCLID 10.2.1-05)
Richtlinie für die amtliche Prüfung von Pflanzenschutzmitteln, Teil IV, 4-1. Biologische Bundesanstalt für Land- und Forstwirtschaft, Germany, December 1986., following GLP, 2	Aerobic primary degradation (compared to OECD 304 and 307)	Dark, 20 °C and moisture level of 40% MWC	Collombey	Loamy Sand	7.2	1.9	0.2 mg/kg corresponding to a field rate of 150 g a.i./ha	362 d	350 d	[pyrrole-^{14}C]-fludioxonil was tested. One metabolite observed (<2.5%)	Minet, U., 1994b (IUCLID 10.2.1-06)
			Les Evouettes	Silty loam	7.3	2.3			342 d		
US EPA subdivision N, para. 162-1 and 162-2[2], following GLP, 2	Aerobic primary degradation (compared to OECD 304 and 307)	Dark, 20 °C and moisture level of 75% FC	Les Evouettes	Silty loam	7.3	2.7	0.2, 0.4 and 0.8 mg/kg corresponding to a field rate of 150, 300 and 600 g a.i./ha	363 d	143 (0.2 mg/kg), 220 (0.4 mg/kg) and 183 days (0.8 mg/kg)	[phenyl-^{14}C]-fludioxonil was tested. One metabolite observed	Minet, U., 1994c (IUCLID 10.2.1-07)

										(<4.9%)	
No guideline cited, following GLP, 2	Aerobic primary degradation (compared to OECD 304 and 307)	Dark, 20 °C and moisture level of 75% FC	Les Evouettes	Silty loam	7.0	2.7	0.048 mg/kg corresponding to a field rate of 36 g a.i./ha	180 d	232 d	[phenyl-^{14}C]-fludioxonil was tested. Unknown radioactivity could be a metabolite (<2.3%)	Reischmann, F.J., 1994 (IUCLID 10.2.1-08)
CGA 192155											
Dutch registration guidelines, Jan 1987, section G 1, Section 6.2.C, following GLP, 2	Aerobic primary degradation (compared to OECD 304 and 307)	Dark, 20 °C, and moisture level of 40% MWC	Gartenacker, CH	Silty loam	7.2	2.0	0.116 mg/kg	73 d	16 d	No metabolites were observed	Ulbrich, R., 1998 (IUCLID 10.2.1-09)
			Pappelacker, CH	Loamy sand	7.4	0.8			24 d		
			Weide, CH	Sandy loam	7.4	1.3			16 d		
CGA 339833											
Dutch registration guidelines, Jan 1987, section G 1, Section 6.2.C, following GLP, 2	Aerobic primary degradation (compared to OECD 304 and 307)	Dark, 20 °C, and moisture level of 40% MWC	Gartenacker, CH	Silty loam	7.2	2.0	0.106 mg/kg	50 d	9.3 d	Non-extractables reached a maximum of 7.2%	Ulbrich, R., 1999 (IUCLID 10.2.1-10)
			Pappelacker, CH	Loamy sand	7.4	0.8			16 d		
			Weide, CH	Sandy loam	7.4	1.3			12 d		

[1] *Test according to OECD criteria*

2 Also guidelines for the official testing of plant protection products, part IV, 4-1, Persistence of plant protection products in the soil – degradation, transformation

Value used in Risk Assessment	
Value/conclusion	Fludioxonil: DT50 values ranges from 143 to 482 days (geomean of 265 days, n= 8, 20 °C). DT50 = 502 days at 12 °C (corrected via Arrhenius equation) CGA 192155: DT50 values ranges from 16 to 24 days (highest value is 24 days, n=3, 20 °C), DT50 = 46 days at 12 °C (corrected via Arrhenius equation) CGA 339833: DT50 values ranges from 9.3 to 16 days (highest value is 16 days, n=3, 20 °C), DT50 = 30 days at 12 °C (corrected via Arrhenius equation)
Justification for the value/conclusion	If up to three values are available the highest value is used. If more than three values are available then the geomean is used. All values are recalculated to 12 °C. Test substance concentrations of 2 mg/kg and higher were not accepted due to possible effects on soil microorganisms as effects were found at this concentration level.

Anaerobic biodegradation

The route and rate of anaerobic degradation of fludioxonil was investigated in soil and associated water in the dark under laboratory conditions at 25ºC (Adam, 1998, IIIA 10.2.1-11). Fludioxonil was shown to be degraded very slowly with a DT50 > 1 year with metabolites, including carbon dioxide, forming less than 1% AR after 392 days. Soil degradation under anaerobic conditions were also investigated in IUCLID 10.2.1-01 and 10.2.1-05. The test 10.2.1-01 was considered unacceptable du to the high test concentration. In the test 10.2.1-05 a DT50 higher than 90 days was found.

Summary table – anaerobic biodegradation in soil- laboratory study											
Method, Guideline, GLP status, Reliability	**Test type[1]**	**Exposure**	**Test system**				**Test substance concentration**	**Incubation period**	**Degradation DT_{50}**	**Remarks**	**Reference**
			Soil origin	Soil type	pH	OC %					
US EPA subdivision N, para. 162-1 and 162-2,	Anaerobic primary degradation	Dark, 25 °C and moisture level of	Madeira, California	Sandy loam	7.5	0.8 OM	0.8 mg/kg corresponding to a field rate of 600 g	392 d	> 392 d	[phenyl-^{14}C]-fludioxonil was	Adam, D., 1998 (IUCLID 10.2.1-11)

following GLP, 2	(compared to OECD 307)	75% FC					a.i./ha			tested. No metabolites were observed (<4.9%)	
[1] *Test according to OECD criteria*											

Value used in Risk Assessment	
Value/conclusion	Fludioxonil: DT50 > 1 year at 25 °C
Justification for the value/conclusion	

4.1.1.3.5.2 Higher tier degradation studies in soil

Data waiving	
Information requirement	Higher tier degradation studies in soil have not been submitted
Justification	[redacted].

4.1.2 Distribution

4.1.2.1 Adsorption onto/desorption from soils

With regard to the findings of a batch adsorption/desorption study, performed with 5 different soils from the UK, fludioxonil exhibits a low potential for mobility in soil. The adsorption constants Ka calculated from the adsorption isotherm according to a Freundlich adsoption relationship range from 290 to 61,000 mL/g (Ka arithmetic mean value; 14,000 mL/g). These values normalized to the content of organic carbon correspond to Koc values between 12,000 and 385,000 mL/g (Koc arithmetic mean value; 145,600 mL/g). No significant influence of the pH was observed (Hawkins, 1991, IUCLID 10.1.2-01).

Summary table – Adsorption/desorption									
Method, Guideline, GLP status, Reliability	**Soil**	**Adsorbed AS [%]**	**K_a (L/kg)**	**K_{aOC} (L/kg)**	**K_d K_{doC} (L/kg)**	**K_a/K_d**	**$1/n_{ads}$ $1/n_{des}$**	**Remarks**	**Reference**
OECD 106, following GLP, 1	Soil 1, Gleadthorpe sand, pH 6.4, 1.7% org. C	98%	770	46,000	3,300 195,000	0.23	0.95 1.11	No degradation products observed, <1% of other components	Hawkins et al., 1991 (IUCLID 10.1.2-01)
	Soil 2, Somersham sandy loam, pH 6.5, 2.4% org. C	98%	290	12,000	650 27,000	0.45	0.81 0.93		
	Soil 3, Sandiacre sandy silt loam, pH 6.9, 3.5% org. C	98%	7,300	210,000	3,500 100,000	2.09	1.14 1.07		
	Soil 4, Goole sandy silt loam, pH 7.9, 2.8% org. C	98%	2,100	75,000	930 33,000	2.26	0.92 0.83		
	Soil 5, Ramsey organic silty clay loam, pH 6.6, 15.8 % org. C	93%	61,000	385,000	K_d not calculated	Could not be calculated	1.19 $1/n_{des}$ is not calculated		

K_a = Adsorption coefficient
K_{aOC} = Adsorption coefficient based on organic carbon content
K_d = Desorption coefficient
K_{dOC} = Desorption coefficient based on organic carbon content
K_a/ K_d = Adsorption / Desorption distribution coefficient

Value used in Risk Assessment	
Value/conclusion	Ka: 14,000 L/kg (arithmetic mean, n=5), Kd: 2,100 L/kg (arithmetic mean, n=4), Kaoc: 145,600 L/kg (arithmetic mean, n=5), kdoc: 89,000 L/kg (arithmetic mean, n=4). No pH dependency
Justification for the value/conclusion	The calculated values are based on a study with 5 soils

4.1.3 Bioaccumulation

Measured aquatic bioconcentration

The measured log Pow of fludioxonil is 4.12 (independent of pH in the range 5 to 9). This indicates a potential for bioaccumulation that requires investigation with a study of bioconcentration behaviour in fish. Furthermore, fludioxonil has a surface tension determined to be 48.5 mN/m and therefore a bioaccumulation study should be conducted according to the "Guidance on Information Requirements". In a bioconcentration study with bluegill sunfish ([redacted]., 1994; IUCLID 9.1.7-02), fludioxonil residues were rapidly concentrated in fish tissues, reaching 95% of the steady-state concentration within two weeks. In edible fish portions, no other radioactivity than ^{14}C-fludioxonil (87.6-93.4%) and non-extractable (3.7-10.6%) could be detected. In non-edible fish portions, ^{14}C-fludioxonil accounted only for 30.2 to 28.0% of the residual radioactivity in the tissue.

Beside the parent molecule, one significant (M2 = 10.7%) and two minor metabolite fractions (MT1 = 4.9% and MT2 = 1.7%) were observed. The metabolite M2 was found at a concentration of 10.7% after 8 days and after 28 days the fraction had decreased to below 8.6%. M2 did not correspond to any of the degradation products: CGA 308565, CGA 192155, CGA 227731 or CGA 257777. Due to the low fractions formed in the study, M2 could not be further characterised by other spectroscopic methods, e.g. MS or NMR. Possibly the metabolite M2 is equal to one of the degradation products formed in water (CGA 339833, CGA 344623 or A5), these metabolites are all included in the risk assessment. As the concentration of the metabolite M2 decreases to below 10% it is not found necessary to investigate this further.
In the study non-extractable radioactivity in non-edible fish portions increased up to 33.4%.

At steady state the estimated bioconcentration factors were of 56 to 58, 741 to 749 and 365 to 366 for edible portions, non-edible portions and whole fish, respectively. Fludioxonil residues were rapidly eliminated following the termination of exposure, with DT_{90} values for the whole fish of <2 days.

In conclusion, fludioxonil showed only limited bioconcentration in bluegill, *Lepomis macrochirus* with a BCF of 366 for whole fish. Bio-concentrated residues were rapidly eliminated following the transfer of fish to fresh water with a DT_{90} of <2 days.

Summary table – Measured aquatic bioconcentration										
Method, Guideline, GLP status, Reliability	**Exposure**	**Log K_{ow} of AS**	**Initial concentration of AS**	**Steady state measured BCF (L/kg wet fish)**	**Uptake rate constant (K_1)**	**Depur. rate constant (K_2)**	**Depur. time (DT_{50})**	**Metabolites**	**Remarks – BCFkinetic (L/kg wet fish)**	**Reference**
US EPA subdivision N, para. 165-4, following GLP, 2	4 weeks uptake followed by 2 weeks depuration	4.12	0.01 mg/L	Edible fish : 58 ; non-edible fish : 741 ; whole fish : 366	Edible fish : 14.0, Non-edible fish : 153, whole fish : 83	Edible fish : 0.248, Non-edible fish : 0.205, whole fish : 0.227	< 2 days	M2=10.7%, MT1=4.9%, MT2=1.7% (Found in non-edible portions)	Edible fish : 56 ; non-edible fish : 749 ; whole fish : 365	[redacted]., 1994 (IUCLID 9.1.7-02)

Value used in Risk Assessment	
Value/conclusion	Edible fish : BCF=58 L/kg wet fish; non-edible fish : BCF=741 L/kg wet fish; whole fish : BCF=366 L/kg wet fish
Justification for the value/conclusion	Steady state BCFs are displayed

Measured and estimated terrestrial bioconcentration

Based on equation 82d in the TGD a BCFearthworm is calculated to be 159 L/kg wet earthworm.

Data waiving	
Information requirement	No measured terrestrial bioconcentration value has been submitted by the applicant. A BCFearthworm has however been calculated to 159 L/kg wet earthworm.
Justification	[redacted]

4.1.4 Monitoring data

No monitoring data have been included.

4.1.5 Fate and distribution of relevant photo-degradation products

In the photo transformation studies in water and soil five relevant photo-transformation products were identified. Different relevant parameters for the substances were found using EPIWEB 4.1 and PBT-profiler[3].
Based on the QSAR estimates it can be seen that the degradation of the photo-degradation products is comparable to fludioxonil or even faster based on the experimental data for CGA 339833 and CGA 192122, however in air half-lives are a little longer. The estimated log Kow and BCF values show that the photo-degradation products have a less tendency to bioaccumulate than fludioxonil. Regarding the mobility all the photo-transformation products seem to be more mobile in soil than fludioxonil and this should be evaluated further in the exposure assessment.

In the PPP assessment of fludioxonil experimental data are provided for a number of endpoints for the degradation products. Not all these data are submitted for the biocide evaluation. Based on a comparison of the experimental data and QSAR estimates it is found sufficient with the QSAR estimates.

[3] Developed by the Environmental Health Analysis Center under contract to the Office of Chemical Safety and Pollution Prevention and U.S. Environmental Protection Agency. http://www.pbtprofiler.net/. Estimates are calculated based on input from BIOWIN v4.10

Substance	Max formation in water (%)	Max formation in soil (%)	SMILIES notation	Mole formula	Molar weight	Vap. Pressure (Pa) 25 deg C	Water solubility (mg/L) 25 deg C	Water solubility (mg/L)	Koc (L/kg)	Koc (L/kg)
							WSKOWWIN	From fragments	MCI method	KOW method
CGA 339833	30.5	9.1	O=C(O)C1(C(#N))C(c2c3c(ccc2)OC(F)(F)O3)(C(=O)(N))O1	C12H6F2N2O6	312.19	3.20E-08	208	56837	10	31
CGA 344623	12.4		c12c(c(C(C(=O)(N))C(C(#N))C(=O)O)ccc1)OC(F)(F)O2	C12H8F2N2O5	298.2	9.33E-08	1091	10767	10	15
A5 (isomer 1)	11.5		c12c(c(CC(C(#N))C(=O)O)ccc1)OC(F)(F)O2	C11H7F2N1O4	255.18	1.68E-04	82	171	22	209
A5 (isomer 2)			c12c(c(C(C(=O)O)CC(#N))ccc1)OC(F)(F)O2	C11H7F2N1O4	255.18	1.68E-04	217	171	22	110
CGA 265378		12.3	O=C1C(c2c3c(ccc2)OC(F)(F)O3)=C(C(#N))C(=O)N1	C12H4F2N2O4	278.17	1.31E-09	7.8	1192	27	2522
CGA 192155		11.7	O=C(O)c1c2c(ccc1)OC(F)(F)O2	C8H4F2=4	202.12	3.88E-02	84	84	10	105

Substance	QSAR estimates via PBT-profiler[1]			QSAR estimate via AOPWIN, KOWWIN v1.68 and BCFBAF		
	DT50 water (days)	DT50 soil (days)	DT50 sediment (days)	DT50 air (hours)	log Kow	BCF (L/kg wet-wt)
Fludioxonil	60	120 (Experimental value: 502 days at 12 °C)	540	6.69	4.12 (Experimental: flask method)	366 (whole fish, experimental) 243 (QSAR estimate based on experimental log Kow)

Substance	QSAR estimates via PBT-profiler[1]			QSAR estimate via AOPWIN, KOWWIN v1.68 and BCFBAF		
	DT50 water (days)	DT50 soil (days)	DT50 sediment (days)	DT50 air (hours)	log Kow	BCF (L/kg wet-wt)
CGA 339833	60	120 (Experimental value: 30 days at 12 °C)	540	9.3	1.68	3.2
CGA 344623	38	75	340	8.1	0.93	3.2
A5	38	75	340	8.0-8.5	3.00 (isomer 1) 2.50 (isomer 2)	3.2
CGA 192155	38	75 (Experimental value: 46 days at 12 °C)	340	52	3.17	3.0
CGA 265378	60	120	540	20	3.58	110

[1] Developed by the Environmental Health Analysis Center under contract to the Office of Chemical Safety and Pollution Prevention and U.S. Environmental Protection Agency. http://www.pbtprofiler.net/. Estimates are calculated based on input from BIOWIN v4.10

4.2 EFFECTS ON ENVIRONMENTAL ORGANISMS

4.2.1 Atmosphere

Fludioxonil has a low vapour pressure of 3.9 x 10^{-7} Pa (at 25ºC) and a low Henry's law constant of ca. 5.4 x 10^{-5} m^3 Pa mol^{-1}. Therefore, volatilisation from soil or water is not expected to be a significant entry route into air for fludioxonil. Based on Atkinson calculation (Stamm, 1999; IUCLID 10.3.1-01), standard conditions, 5 x 10^5 OH radicals/cm^3, 24 hour day, the photochemical oxidative degradation in air would proceed with a half-life of 6.7 hours (3.6 hours for a 12 hour day, 1.5 x 10^6 OH radicals/cm^3). Referring to these results, an accumulation of fludioxonil in air is not expected.

4.2.2 Sewage treatment plant (STP)

Inhibition of microbial activity (aquatic)

The inhibition effect of fludioxonil on the respiration rate of aerobic wastewater microorganisms of activated sludge was investigated in a 3-hour respiration inhibition test according to the OECD Guideline for testing of chemicals No. 209 (Weinstock, M., 1994, IUCLID 9.1.5-01). The nominal test concentrations used in the test were 14.5, 22, 39.5, 62 and 102 mg/L. All of them are far above the water solubility of 1.8 mg/L of fludioxonil. As no inhibiton is observed at the highest test concentration, the NOEC is set equal to the water solubility of 1.8 mg/L. This endpoint will therefore be used for the PNEC derivation. The test substance concentrations were not confirmed by analytical methods.

Summary table – inhibition of microbial activity									
Method, Guideline, GLP status, Reliability	**Species/ Inoculum**	**Endpoint**	**Exposure**		**Results**			**Remarks**	**Refe-rence**
			Design	**Duration**	**EC_{20}**	**EC_{50}**	**EC_{80}**		
OECD 209, GLP is followed, 2	Activated sludge	Oxygen consumption	Inhibition of respiratory rate	3 hours	All test concentrations are above the water solubility			Solubility was exceeded. NOEC = 1.8 mg/L	Weinstock, M., 1994 (IUCLID 9.1.5-01)

Value used in Risk Assessment	
Value/conclusion	NOEC = 1.8 mg/L; PNEC =0.18 mg/L (AF of 10)
Justification for the value/conclusion	No inhibition of oxygen consumption of aerobic sewage treatment bacteria was seen with the tested concentrations of fludioxonil therefore NOEC is set equal to the water solubility of fludioxonil

4.2.3 Aquatic compartment

4.2.3.1 Freshwater compartment

Acute toxicity (freshwater and marine)

The acute toxicity of fludioxonil to fish was investigated in laboratory tests with two freshwater and one marine fish species. The LC_{50} values were found to be in a range of 0.23 to 1.2 mg/L.

The acute toxicity of fludioxonil to aquatic invertebrates was investigated in two laboratory tests with one freshwater species (*Daphnia*). The EC_{50} values for the fresh water *Daphnia magna* were found to be in a range of 0.40 – 0.90 mg/L.

The effects of fludioxonil on green algae were determined on two algae species. The lowest E_rC_{50} value was found to be 0.21 mg/L after 48 hours of exposure. Results for algae are all based on 48 hour exposure and geomean measured concentrations (0-72 h and 0-120 h) due to excessive pH variation at 72 and 120 hours of exposure. In the PPP assessment results for 72 and 120 h were accepted eventhough excessive pH variation took place. The most sensitive organism in the short term toxicity tests is green algae (*Pseudokirchneriella subcapitata*, formerly known as *Selenastrum capricornutum*)

Summary table – acute aquatic toxicity									
Method, Guideline, GLP status, Reliability	**Species**	**Endpoint**	**Exposure**		**Results**			**Remarks**	**Reference**
			Design	**Duration**	**LC/EC$_0$**	**LC/EC$_{50}$**	**LC/EC$_{100}$**		
Fish									
EPA 72-1, following GLP, 2	Rainbow trout (*Oncorhynchus mykiss*)	96 h LC_{50}	Flow-through test	96 h	0.26 mg/L (m)	0.47 mg/L (95% c.l. of 0.38-0.69 mg/L)	0.71 mg/L		[redacted] 1993a (IUCLID 9.1.1-01)
EPA 72-1, following GLP, 2	Rainbow trout (*Oncorhynchus mykiss*)	96 h LC_{50}	Flow-through test	96 h	0.11 mg/L (m)	0.23 mg/L (95% c.l. of 0.18-0.33 mg/L)	0.33 mg/L		[redacted] 1997a (IUCLID 9.1.1-02)

EPA 72-1, following GLP, 2	Bluegill sunfish (*Lepomis macrochirus*)	96 h LC_{50}	Flow-through test	96 h	0.45 mg/L (m)	0.74 mg/L (95% c.l. of 0.62-0.96 mg/L)	0.96 mg/L		[redacted] 1997b (IUCLID 9.1.1-03)
EPA 72-1, following GLP, 2	Sheepshead minnow (*Cyprinodon variegatus*)	96 h LC_{50}	Flow-through test	96 h	0.93 mg/L (m)	1.2 mg/L (95% c.l. of 0.93-1.5 mg/L)	1.5 mg/L	Marine The LC50 is calculated based on 100% mortality at 1.5 and 0% mortality at 0.93 mg/L.	[redacted] 1993b (IUCLID 9.1.1-04)
Invertebrates									
EPA 72-2, following GLP, 1	Daphnids (*Daphnia magna*)	48 h EC_{50}	Flow-through test	48 h	<0.21 mg/L (m)	0.40 mg/L (m)	>0.76 mg/L (m)	Slight immobility was observed in the lowest concentrations (0.12 and 0.21 mg/L).The EC_0 is therefore not considered relevant.	Surprenant, D.C., 1990 (IUCLID 9.1.2-01)
EPA 72-2, following GLP, 1	Daphnids (*Daphnia magna*)	48 h EC_{50}	Flow-through test	48 h	<0.50 mg/L (m)	0.90 mg/L (m)	1.9 mg/L (m)	Immobility was observed in the lowest test concentrations.The EC_0 value therefore not considered relevant.	Holmes and Swigert, 1993c (IUCLID 9.1.2-02)

Algae (growth inhibition)					**NOE_rC or E_rC_{10}**	**E_bC_{50}[1]**	**E_rC_{50}[2]**		
OECD 201, following GLP, 2	Green algae (*Desmodesmus subspicatus*)	48 h EC_{50}	Static test	72 h	0.09 mg/L (m)	>0.926 mg/L (m)		Results are based on 48 h value due to excessive pH variation in the test.	Rufli, H., 1989a (IUCLID 9.1.3-01)
FIFRA 122-2 and 123-2, following GLP, 2	Green algae (*Pseudokirchneriella subcapitata*)	48 h EC_{50}	Static test	120 h	0.027 mg/L (m)		0.21 mg/L (m)	Results are based on 48 h value due to excessive pH variation in the test.	Hoberg, J.R., 1992 and 2005 (IUCLID 9.1.3-02)

[1] calculated from the area under the growth curve

[2] calculated from growth rate

(n): nominal value

(m): measured value

Data waiving	
Information requirement	Effects on growth rate of cyanobacteria or diatoms
Justification	[redacted]

Chronic toxicity (freshwater)

A series of flow-through chronic fish studies have been conducted. The lowest reliable endpoint obtained is a NOEC of 0.04 mg/L from an OECD 215 study with Rainbow trout. In a fathead minnow early life stage toxicity test, mean length and weight and survival at 28 day post-hatch were the most sensitive biological parameters. Based on these observations, the overall chronic NOEC for fish was determined to be 0.039 mg/L. In three earlier studies that followed an outdated test design ([redacted], 1993 a ,b ,c), difficulties were encountered in dosing and keeping stable exposure concentrations. The findings reported for these studies are consequently considered to be unreliable and have not been used in the assessment.

Three chronic toxicity studies were conducted with *Daphnia magna*. In the study by Putt, A. E. (1991), the most sensitive biological parameters indicating effects of fludioxonil were the number of offspring/female and the mean body length. The overall NOEC of this study was established to be 0.019 mg/L. In a second test by Rufli, H. (1989c), the fraction of dead young and the time for appearance of first brood were the most sensitive biological parameters. The overall NOEC of this test was determined to be 0.005 mg/L. In this test a surfactant was added to aid the solubilisation of the test substance, it is not clear if this surfactant (an alkylphenol derivative) might have influenced the results. Due to a high number of defiencies in the study a reliability factor of 3 is given. Find the explanation in the annotations for the study. In the newest study by Fournier, A. E. (2014) performed according to OECD 211, an overall NOEC of 0.035 mg/L (mean measured concentration) was found for reproduction, mortality and growth. This study is given a reliability factor of 1 as it fulfils all the validity criteria given in the OECD 211 guideline. The result from this study is considered as more reliable compared to the results from the other study as the study by Fournier, A. E. (2014) is fully performed according to OECD 211 and as measured concentrations are quite stable during the test period whereas there is a high variation in the measured concentrations of the two other tests.

Summary table – chronic aquatic toxicity							
Method, Guideline, GLP status, Reliability	**Species**	**End point/ Type of test**	**Exposure**		**Results (mg/L)**	**Remarks**	**Reference**
			Design	**Duration**	**LOEC/NOEC/ EC_{10}**		
Fish							
OECD 204, GLP followed, 3	Rainbow trout (*Oncorhynchus mykiss*)	Mortality and other observed effects	flow-through	21 day	NOEC = 0.014* (n)	* the result shall not be used in the assessment	[redacted], 1993a (IUCLID 9.1.6.1-01)
OECD 204, GLP followed, 3	Rainbow trout (*Oncorhynchus mykiss*)	Mortality and other observed effects	flow-through	21 day	NOEC = 0.011* (n)	* the result shall not be used in the assessment	[redacted]., 1993b (IUCLID 9.1.6.1-02)
OECD 204, GLP followed, 3	Rainbow trout (*Oncorhynchus mykiss*)	Mortality and other observed effects	flow-through	21 day	NOEC = 0.01* (n)	* the result shall not be used in the assessment	[redacted]., 1993c (IUCLID 9.1.6.1-03)
OECD 215, GLP followed, 1	Rainbow trout (*Oncorhynchus mykiss*)	Mortality and growth (juvenile growth test)	flow-through	28 day	NOEC = 0.040 (n, m)		[redacted] 2005 (IUCLID 9.1.6.1-04)
US EPA FIRFA	Fathead	Lethal and sub-	flow-	28 day –	NOEC =		[redacted] 1994

540/9-82-024, US EPA-OPP 540/9-86-138, ASTM 1241-88 (OECD 210), GLP followed, 2	minnow (*Pimephales promelas*)	lethal effects of early-life stages	through	early life stage	0.039 (m)		(IUCLID 9.1.6.1-05)
Invertebrates							
US EPA 5401-85-024 (OECD 211), GLP followed, 2	*Daphnia magna*	Mortality, reproduction and growth	flow-through	21 days	NOEC = 0.019 (m)	Lowest NOEC in the test.	Putt, A.E., 1991 (IUCLID 9.1.6.2-01)
OECD 202 (OECD 211), GLP followed, 3	*Daphnia magna*	Mortality, reproduction and growth	semi-static	21 days	NOEC = 0.005 (m)	Lowest NOEC in the test. * the result shall not be used in the assessment	Rufli, H., 1989c (IUCLID 9.1.6.2-02)
OECD 211, GLP followed, 1	*Daphnia magna*	Mortality, reproduction and growth	semi-static	21 days	NOEC = 0.035 (m)	NOEC for reproduction, mortality and growth	Fournier, A.E., 2014 (IUCLID 9.1.6.2-03)
(n): nominal value (m): measured value							

4.2.3.2 Higher tier studies on aquatic organisms

Microcosm study

An outdoor aquatic microcosm study (Giddings, 1993; IUCLID 9.1.8-01) was conducted to study the environmental fate and ecological effects of fludioxonil on aquatic organisms following five repeated applications at 14-day intervals. Nominal concentrations were: 0 (control), 3.0, 8.2, 16.4, 32.8 µg/L.

Periphyton abundance and taxonomic richness were significantly reduced at all treatment levels on one occasion near the end of the treatment period. Periphyton data were highly variable, and the effects did not appear on later sampling events. Chrysophytes and diatoms in the phytoplankton were affected by fludioxonil at the highest single treatment level of nominally 32.8 µg/L. Green and blue green algae were not reduced (blue green algae may have increased at the highest treatment level).

Among the zooplankton, only the rotifer *Keratella* showed consistent effects of treatment with fludioxonil at the highest single treatment level of nominally 32.8 µg/L.

Macro invertebrates may have been reduced at the highest treatment level near the end of the study, but there were few statistically significant differences in macroinvertebrate abundance. Bluegill sunfish survival and growth were unaffected by fludioxonil treatment.

Overall, the impact of fludioxonil on the microcosm communities was minor, and occurred mainly at the lowest trophic level (phytoplankton and periphyton). Secondary effects may have occurred on the rotifer Keratella. Densities of benthic macroinvertebrates might have been reduced near the end of the study at the highest single treatment level of nominally 32.8 µg/L. Fish were unaffected.

The study is found to meet the criteria for being reliable according to paragraph 3.1.2 in DRAFT Guidance document for the use of aquatic model ecosystem studies for biocides (2013). However, only few effects are seen during the study, this might be due to fast degradation of fludioxonil by photolytic decomposition while the sunlight penetrated to the bottom of the tanks during most of the study.

The current microcosm study address effects on a broad range of species. Fludioxonil is a fungicide and based on laboratory effect data, algae (*Pseudokirchneriella subcapitata*) and fish (rainbow throut) seems to be the most sensitive species regarding acute effects and crustaceans (*Daphnia magna*) and algae (*P. subcapitata*) seems to be the most sensitive species regarding chronic effects. All groups of organisms are present in the microcosm study.

The exposure regime of the microcosm study (treatment 5 times with 2 weeks interval) is not relevant for the biocide exposure which for the applied use results in a continuous exposure from sewage treatment plants. Therefore recovery is also not relevant for the biocide use where the exposure is continuous.

The study is found acceptable (given a reliability factor of 2). A calculation of a no observed ecologically-adverse effect concentration (NOAEC) for fludioxonil is 16.4 µg/L (nominal concentration) and geomean of 20.3 µg/L (corresponding to the geomean measured fludioxonil concentration for the five treatments). The study will not be used for lowering the AF as there is no evidence of a most sensitive species in the microcosm. Furthermore fish were introduced in the study and these are known for disturbing the biological processes and results are therefore not considered.

Value used in Risk Assessment	
Value/conclusion	NOEC = 0.019 mg/L (m) (*Daphnia magna*, 21 days) PNEC = 0.0019 mg/L
Justification for the value/conclusion	The lowest long term aquatic NOEC is for dapnia. This result will therefore be used for PNEC derivation. An AF of 10 is applied

4.2.3.3 Sediment compartment

Long-term toxicity test

Toxicity test of fludioxonil on sediment-dwelling *Chironomus riparius* indicated that the compound is of low toxicity to this organism with NOEC values of 160 and 40 mg/kg dry sediment.

Summary table – long-term toxicity to sediment dwelling organisms							
Method, Guideline, GLP status, Reliability	**Species**	**Endpoint/ Type of test**	**Exposure**		**Results**	**Remarks**	**Reference**
			Design	**Duration**	**LOEC/NOEC/EC_{10}**		
OECD 218, according to GLP, 2	*Chironomus riparius* larvae	Emergence rate, development rate, effects on emerged midges	Static (spiked sediment)	28 days	NOEC = 160 mg/kg dry sediment (n) for emergence rate and development rate and NOEC= 40 mg/kg dry sediment (n) for effects on emerged midges		[redacted]., 1998 (IUCLID 9.1.9-01)
(n): nominal value							

Value used in Risk Assessment	
Value/conclusion	NOEC = 40 mg/kg dry sediment (n) (8.70 mg/kg wet sediment). PNEC = 0.40 mg/kg dry sediment (0.0870 mg/kg wet sediment)
Justification for the value/conclusion	The lowest effect value is chosen for the risk assessment. As only one long-term test is available an assessment factor of 100 is used.

4.2.3.4 Marine compartment

Data waiving	
Information requirement	Effects on marine aquatic species.
Justification	[redacted]

4.2.4 Terrestrial compartment

Toxicity to terrestrial organisms, acute tests

The results of toxicity tests in artificial soil show that fludioxonil is of low toxicity to earthworms, with an acute LC_{50} >1000 mg/kg dry soil (see Table 4.2.5). Two studies with fludioxonil on soil microorganism activity were conducted on different soil types. In the first study conducted on a sandy silty loam and a sand soil (Schanne, 1992; IUCLID 9.2.1-01), for both soil types fludioxonil showed only negligible, not significant effects on soil respiration at concentrations up to 1.3 mg/kg dry soil. In the sandy soil, the compound caused negligible to tolerable effects on the nitrification process at low and high dose treatments. These effects decreased with time. No marked differences in total N-mineralisation could be observed up to 1.3 mg/kg dry soil. In the sandy silt loam soil, the effects of fludioxonil on soil activity were more marked. Upon extension of incubation up to 97 days, the observed effects lay in the critical zone in the Malkomes 12 scheme. The inhibitory effects show a decreasing trend. At the end of the test period of 97 days the deviations were <25% from the control at up to 1.3 mg/kg dry soil.

In the second study conducted on a sandy loam soil and a loam soil (Wüthrich, 1993; IUCLID 9.2.1-02), for both soil types fludioxonil showed negligible effects in short-term respiration experiments up to a concentration of 0.333 mg fludioxonil /kg dry soil weight. Furthermore, it was shown that neither the ammonification nor the nitrification processes were significantly affected by the compound. At the end of the incubation phase of 28 days the effects of fludioxonil on soil activity deviated by <25% from the controls at up to 0.333 mg/kg dry soil weight. The two studies on soil microorganism (IUCLID 9.2.1-01 and 9.2.1-02) are not considered valid as they are performed with a pesticided at only two testconcentrations representing field dose. Therefore it is not possible to use them for calculating effect concentrations.
A study determining the effects of fludioxonil on the growth of soil fungi was performed on *Mucor circinelloides* var. *griseocyanus*, *Marasmius oreades*, *Phytophthora nicotianae* and *Paecilomyces marquandii* (Grade, 2002; IUCLID 9.2.1-03). The lowest EC_{50} value determined for these soil fungi was >1.68 mg/kg dry soil.
Soil incorporation of a fludioxonil formulation were tested in two studies and no effects on the seedling emergence of a number of different plants were seen up to 21 days after planting (Porch, 2002; IUCLID 9.2.3-01)(Porch et al, 2011; IUCLID 9.2.3-02). The LC_{50} values for the product were determined to be greater than 8.46 mg a.s./kg dry soil (corrected to standard organic matter of 3.4%).

Summary table – acute terrestrial toxicity										
Method, Guideline, GLP status, Reliability	**Species**	**End point/ Type of test**	**Exposure**		**Organic carbon content**	**Results (mg/kg dry weight)**			**Remarks**	**Reference**
			Design	**Duration**		**LC/EC_0**	**LC/EC_{10}**	**LC/EC_{50}**		
Earthworm/soil-dwelling non-target invertebrates										
OECD 207,GLP followed, 2	*Eisenia foetida*	Mortality	In exposed artificial soil	14 days	10% OM	111 (n)	Could not be calculated	>1000 (n)	No correction to standard soil	Rufli, H., 1989b (IUCLID 9.2.2-01)
Soil microflora										
BBA Teil VI 1-1 (2nd edition), GLP followed, 3	Soil microorganisms	Respiration and nitrification	Test concentrations: 0.13 and 1.3 mg/kg dry soil	Respiration: 28 days, Nitrification: 97 days	1.2% OC (F3) and 0.70% OC (2.1)	>1.3 (n)*	>1.3 (n)*	>1.3 (n)*	Use as supportive information	Schanné and Galicia, 1992 (IUCLID 9.2.1-01)
BBA Teil VI 1-1 (2nd edition), GLP followed, 3	Soil microorganisms	Mycelium growth	Test concentrations: 0.067 and 0.333 mg/kg dry soil	Respiration: 28 and 30 days, Nitrification: 28 days	Soil I: 0.588 to 1.34% OC Soil II: 1.61% OC	>0.333 (n)*	>0.333 (n)*	>0.333 (n)*	Use as supportive information	Wüthrich, 1993 (IUCLID 9.2.1-02)
OECD 216 and 217, GLP followed, 2	4 species of fungi	Respiration and nitrification	Six concentrations were included	3-15 days	0.91% OC	0.168 (n) 1.68 (n) 0.0504 (n) 0.0168 (n)	Has not been calculated	6.9 (n) >1.68 (n) 3.7 (n) 8.9 (n)	EC50 of >1.68 mg/kg dry soil corresponds to >3.69[A] mg/kg dry soil	Grade, R., 2002 (IUCLID 9.2.1-03)
Non target plants										

OECD 208, GLP followed, 2	*Triricum aestivum, Lactuca sativa, Raphanus sativus*	Seedling emergence and weight reduction	In exposed artificial soil	18 days	1.9% OM	0.261 (n) (0.467[A])	Could not be calculated	>0.261 (n) (>0.467[A])	The test material is a product containing 2.61% fludioxonil	Porch and Krueger, 2002 (IUCLID 9.2.3-01)
OECD 208, GLP followed, 2	*Raphanus sativus, Lycopersicon esculentum, Lactuca sativa, Glycine max, Brassica oleracea, Beta vulgaris, Zea mays, Triticum aestivum, Allium cepa, Lolium perenne*	Seedling emergence and weight reduction	In exposed artificial soil	21 days	0.71% OC (1.2% OM)	2.987 (n) (8.46[A])	Could not be calculated	>2.987 (n) (>8.46[A])	The test material is a product containing 50.4% fludioxonil	Porch et al., 2011 (IUCLID 9.2.3-02)

(n): nominal value

* Results from the studies can not be used for PNEC setting as dose response relationships could not be established as only two concentrations were included in each study

[A] After conversion to the TGD standard organic matter content of 3.4%

Toxicity to terrestrial organisms, chronic tests

Fludioxonil was shown to be of low toxicity to adult earthworms and did not significantly affect their reproduction performance after prolonged exposure. A chronic earthworm toxicity study was performed in which earthworms were exposed to fludioxonil homogeneously mixed in the artificial soil at concentrations up to 20 mg a.s./kg dry soil.

Summary table – long term terrestrial toxicity							
Method, Guideline, GLP status, Reliability	**Species**	**End point/ Type of test**	**Exposure**		**Results**	**Remarks**	**Reference**
			Design	**Duration**	**LOEC/NOEC/EC_{10}** (mg/kg dry soil)		
Earthworm/soil-dwelling non-target invertebrates reproduction							
ISO 11268-2 (OECD 222), GLP followed, 2	*Eisenia fetida*	Mortality, growth and reproduction	In exposed artificial soil	28 days + 28 days	NOEC (mortality and reproduction) = 20 (n)	No correction to standard soil	Friedrich, S., 2003 (IUCLID 9.2.2-02)
(n): nominal value							

Value used in Risk Assessment	
Value/conclusion	EC50 > 3.69 mg/kg dry soil (n) (fungal mycelial growth – corrected to the TGD standard organic matter content of 3.4%) PNEC = 0.0369 mg/kg dry soil
Justification for the value/conclusion	Acutely, plants are the potentially most sensitive species but the plant EC_{50} (>8.46 mg/kg dry soil) is significantly lower than the NOEC from the long-term earthworm study (20 mg/kg dry soil) and possibly also lower than the NOEC from the nitrification study (supported by the study on 28 days) where NOEC is found to be above 1.3 mg/kg dry soil (no correction to standard soil is performed). An assessment factor of 100 should be applied to the lowest L(E)C50 (in analogy to the PNEC derivation for aquatic compartment). The lowest endpoint is found to be EC50 > 3.69 mg/kg dry soil (n) (mycelial growth– corrected to the TGD standard organic matter content of 3.4%). The PNEC will therefore be 0.0369 mg/kg dry soil. This is situation 3 for the clarification on the assessment factor to derive PNECsoil.

Data waiving	
Information requirement	Effects on honeybees and on other non-target terrestrial arthropods
Justification	[redacted]

4.2.5 Groundwater

No test data or monitoring data in groundwater are available.

4.2.6 Birds and mammals

Data waiving	
Information requirement	Effects on birds
Justification	[redacted]

4.2.7 Primary and secondary poisoning

Data waiving	
Information requirement	Primary and secondary poisoning
Justification	[redacted]

4.2.8 Ecotoxicity of relevant photo-degradation products

In the photo transformation studies in water and soil five relevant photo-transformation products were identified in concentrations above 10% of AR. By using EPIWEB 4.1 QSAR estimates of aquatic effect values could be found, these data are shown below. By comparing the estimated effect concentrations of the photo-degradation products to the estimated and lowest experimental effect concentrations of fludioxonil it can be concluded that the photo-degradation products are less toxic than fludioxonil. The photo-degradation product CGA 192155 however seems to have comparable ecotoxicity to fludioxonil. Based on the data below and the fact that structures of the photo-degradation products are similar to fludioxonil and all having lower Kow values than fludioxonil, it is therefore found that the photo-degradation products are covered by the effect assessment of fludioxonil, it is found that this conclusion is applicable for organisms in all the environmental compartments that are assessed. This conclusion is also reported in the EFSA conclusion for fludioxonil (2007). PNEC values for fludioxonil (presented in section 4.4) will therefore also be used for all the identified photo-transformation products.

Summary table – QSAR estimates for aquatic toxicity							
Organism, endpoint	**Fludioxonil**		**CGA 339833**	**CGA 344623**	**A5 (2 isomers)**	**CGA 192155**	**CGA 265378**
	Experimental data[1] (mg/L)	**QSAR estimate[2] (mg/L)**					
Fish, 96h LC50	0.23	0.14	448	1837	28	2.0	16
Daphnid, 48h LC50	0.40	0.28	59	132	11	0.61	11
Green algae, 96h EC50	0.21 (48h)	0.44	8.4	13	12	0.22	7.4
Fish, ChV	0.039 (NOEC)	0.101	0.32	16	2.6	0.012	1.5
Daphnid, ChV	0.019 (NOEC)	0.000834	4.7	9.8	0.97	0.026	0.64
Green Algae, ChV	0.027 (NOEC)	0.246	5.2	5.0	5.1	0.327	3.3

1: lowest value

2: lowest value estimated by Ecosar v1.11

3: ChV – Chronic value is defined as the geometric mean of the no observed effect concentration (NOEC) and the lowest effect concentration (LOEC). This can be mathematically represented as: ChV=10^(log(LOEC x NOEC)/2)

4.3 ENDOCRINE DISRUPTING PROPERTIES

Fludioxonil is not listed in the document of the EU Commission on endocrine disrupting chemicals (COMMISSION STAFF WORKING DOCUMENT on implementation of the Community Strategy for Endocrine Disrupters - a range of substances suspected of interfering with the hormone systems of humans and wildlife (COM (1999) 706)).

The submitted toxicological dossier evaluated for fludioxonil does not indicate a endocrine disruption potential of the substance. Fludioxonil does not cause adverse effects in a whole/healthy organism in available *in vivo* studies (repeated dose toxicity, 2-generation reproductive toxicity study). The target organs are the liver and kidney. The available *in vivo* reproduction toxicity study and other chronic toxicity studies do not show any signs of (anti)estrogenic/androgenic activity.

Teng *et al* (2013)[4] report that fludioxonil increases the expression of the microRNA miR-21 in the MCF-7 human breast cancer cell line at concentrations of between 10-1000 nM, through transcriptional (primary) and secondary mechanisms. Investigation of other microRNA types revealed that fludioxonil increased expression of some (miR-200a) and reduced the expression of others (miR-125b, miR-181), leading the authors to suggest that the effects on miR-21 are not due to a general increase in miRNA expression. Increased expression of miR-21 in response to fludioxonil (10-100 nM) was also seen in the T47D human breast cancer cell line but not in a normal breast cell line (MCF-10A) or in an oestrogen non-responsive breast cancer cell line (MDA-MB-231). This spectrum of response indicates that the effects of fludioxonil are not cell-line specific, but may be related to ERα expression. Expression of pri-miR-21 (the precursor of miR-21) in MCF-7 cells was increased in the presence of fludioxonil (100 nM) and was also increased by exposure to DHT but not oestradiol. The response to fludioxonil but not DHT was blocked by actinomycin D, suggesting an effect of fludioxonil on transcription. Consistent with the effect on miR-21, fludioxonil reduced PTEN and BCl2 protein levels. The authors suggest that the effects of fludioxonil are mediated through activation of the androgen and oestrogen receptors.

As miR-21 is postulated to have a role in breast cancer (it is overexpressed in breast cancer cell lines and is associated with reduced survival time), the authors suggest that exposure to fludioxonil may influence the development of breast cancer in exposed populations. It is notable in this respect, that the carcinogenicity of fludioxonil has been investigated in studies in the rat at dietary concentrations of up to 1000 ppm (141 mg/kg bw/d) and in mouse at dietary concentrations of up to 7000 ppm (~1000 mg/kg bw/d). These studies do not indicate any effects on the development of breast cancer; evaluations by EFSA and the WHO JMPR conclude that the studies provide no evidence of carcinogenicity. The comprehensive toxicological dataset for fludioxonil similarly does not identify any effects on reproduction, development, organ weights or pathology indicative of an endocrine mode of action. The EFSA conclusion notes that the target organs of fludioxonil toxicity are the liver and kidney.

The results of the published study of Teng *et al* (2013) are stated by the authors to indicate effects mediated by fludioxonil *via* activation of the androgen and oestrogen receptors. Effects are reported at a subcellular (molecular) level in a non-validated test system. MicroRNA research is a relatively new field and the implications of changes in microRNA expression in human disease are not fully elucidated.

4 *Teng Y, Manavalan TT, Hu C, Medjakovic S, Jungbauer A & Klinge CM (2013). Endocrine disruptors fludioxonil and fenhexamid stimulate miR-21 expression in breast cancer cells. Toxicological Sciences 131(1):71-83.*

Attributing a potential health outcome to the effects of fludioxonil reported in this study is therefore somewhat speculative. The relevance of the fludioxonil concentration of 100 nM investigated in the Teng *et al* (2013) study to likely concentrations attained in human tissues following occupational or dietary exposure is unclear; it is notable that the study reports effects of fludioxonil on cell viability, although these effects are not discussed further.

In a recent article published in Nature Communications[5] fludioxonil was clustered together with other oestrogenic compounds in the first comprehensive analysis of the Tox21 effort, a large scale *in vitro* toxicity screening of chemicals. Compound clustering by structure similarity and activity profile similarity across the assays reveals structure–activity relationships that are useful for the generation of mechanistic hypotheses. The second phase of Tox21 program involves testing a collection of more than 10,000 compounds (Tox21 10K library). The initial focus was on creating assays to test the compounds' effects on nuclear receptors (AhR, AR, ERα, FXR, GR, PPARδ, PPARγ, TR and VDR) and stress response pathways (p53, NF-κB, pH2AX, endoplasmic reticulum stress, mitochondrial membrane potential, ARE/Nrf-2, heat shock response and DNA damage). The 10 K compounds were grouped into 610 clusters by their activity profile similarity and each cluster was examined for enriched Medical Subject Headings (MeSH; **http://www.ncbi.nlm.nih.gov/mesh**) pharmacological action (PA) terms. The results indicated that compounds with similar activity profiles as determined in the Tox21 screens tend to share similar annotated modes of action (MOAs).

The effects reported in the published study and the Tox21 program also have to be considered in light of the absence of endocrine-related findings in the standard *in vivo* mammalian toxicity studies. It is too early to concluded that the findings in the study give raise to specific concerns of relevance to endocrine disruption by fludioxonil *in vivo*.

There is consequently no cause to consider that fludioxonil nor the degradation products may interfere with the hormone systems of wildlife.

4.4 DERIVATION OF PNECS

The following PNEC values will be used for the risk assessment of fludioxonil and for the photo-transformation products as explained in section 4.2.8 as this is considered as a worst case.

5 *Ruili Huang at al. (2016). Modelling the Tox21 10 K chemical profiles for in vivo toxicity prediction and mechanism characterization. Nature Communications Volume: 7, Article number: 10425 DOI: doi:10.1038/ncomms10425. Published26 January 2016*

Compartment	PNEC	Remarks/Justification
Freshwater	*$PNEC_{freshwater}$: 0.0019 mg/L*	Organism: *Daphnia magna* Endpoint: *NOEC (21 d) = 0.019 mg/L* Assessment factor: *10* Extrapolation method: *Assessment factor* Justification: *Since long term NOECs from three trophic levels (fish, invertebrates, algae) are available, an assessment factor of 10 can be used.*
Sewage treatment plant (STP)	*$PNEC_{STP}$: 0.18 mg/L*	Organism: *Sewage sludge bacteria* Endpoint: *NOEC = 1.8 mg/L* Assessment factor: *10* Extrapolation method: *Assessment factor* Justification: *No inhibition of oxygen consumption of aerobic sewage bacteria was seen with the tested concentrations of fludioxonil. therefore NOEC is set equal to the water solubility of fludioxonil.*
Sediment	*PNECsediment: 0.40 mg/kg dry sediment (0.0870 mg/kg wet sediment)*	Organism: *Chironomus riparius* Endpoint: *NOEC (28 d) = 40 mg/kg dry sediment* Assessment factor: *100* Extrapolation method: *Assessment factor* Justification: *The lowest effect value is chosen for the risk assessment. As only one long-term test is available an assessment factor of 100 is used.*
Soil	*PNECsoil: 0.0369 mg/kg dry soil*	Organism: *nitrogen mineralization test* Endpoint: *EC50 (15 d) > 3.69 mg/kg dry soil* Assessment factor: *100* Extrapolation method: *Assessment factor* Justification: *Situation 3 for choice of assessment factor for PNECsoil derivation from infobox 10 in the "Guidance on Environmental Risk Assessment – Active Substance" (DRAFT)*

5 ASSESSMENT OF EXCLUSION CRITERIA, SUBSTITUTION CRITERIA AND POP

5.1 EXCLUSION CRITERIA

5.1.1 Assessment of CMR properties

Criteria (BPR Article 5[1])	**Assessment**
Active substances which have been classified in accordance with Regulation (EC) No 1272/2008 as, or which meet the criteria to be classified as, carcinogen category 1A or 1B	Fludioxonil is not classified for human health and does not meet the criteria to be classified as Carc. Cat. 1A or 1B.
Active substances which have been classified in accordance with Regulation (EC) No 1272/2008 as, or which meet the criteria to be classified as, mutagen category 1A or 1B	Fludioxonil is not classified for human health and does not meet the criteria to be classified as Muta. Cat. 1A or 1B.
Active substances which have been classified in accordance with Regulation (EC) No 1272/2008 as, or which meet the criteria to be classified as, toxic for reproduction category 1A or 1B	Fludioxonil is not classified for human health and does not meet the criteria to be classified as Repr. Cat. 1A or 1B.

Conclusion on CMR properties	The exclusion criteria in BPR Article 5(1)a-c are not met.

5.1.2 Assessment of endocrine disrupting properties

Criteria (BPR Article 5)	**Assessment**
Active substances which, on the basis of the criteria specified pursuant to the first subparagraph of paragraph 3 are considered as having endocrine-disrupting properties that may cause adverse effects in humans and to the environment.	The criteria are not yet published.

Criteria (BPR Article 5)	**Assessment**
Pending the adoption of those criteria[1], active substances that are classified in accordance with Regulation (EC) No 1272/2008 as, or meet the criteria to be classified as, carcinogen category 2 and toxic for reproduction category 2[2].	Fludioxonil is not classified for human health and does not meet the criteria to be classified as Carc. Cat. 2 or Repr. Cat. 2. Fludioxonil has not been shown to have toxic effects on endocrine organs in standard mammalian *in vivo* studies.
Substances such as those that are classified in accordance with Regulation (EC) No 1272/2008 as, or that meet the criteria to be classified as, toxic for reproduction category 2 and that have toxic effects on the endocrine organs[3].	Fludioxonil is not classified for human health and does not meet the criteria to be classified as Carc. Cat. 2. Fludioxonil has not been shown to have toxic effects on endocrine organs in standard mammalian *in vivo* studies.
Active substances which are identified in accordance with Articles 57(f) and 59(1) of Regulation (EC) No 1907/2006 as having endocrine disrupting properties	Active substance has not been identified as having endocrine disrupting properties *in vivo.*

[1] This refers to the criteria mentioned in the first row.
[2] These active substances shall be considered as having endocrine-disrupting properties
[3] These active substances may be considered as having endocrine-disrupting properties

Conclusion on ED properties	The exclusion criteria in BPR Article 5(1)d are not met. Therefore, the interim criteria for endocrine disruptors are not met.

5.1.3 PBT Assessment (following Annex XIII to Regulation (EC) No 1907/2006)

Assessment of persistence

Screening

Fludioxonil

Fludioxonil is not readily biodegradable and there is no evidence of hydrolysis. Fludioxonil is readily degraded by photolysis in water and in soil with half-lifes of 9.3 and 9.5 days (26 and 27 days at 12 °C), respectively. A number of major photolysis products are formed, in water they were identified as CGA 339833 (max. 30.5% AR), CGA 344623 (max. 12.4% AR) and A5 at 11.5% AR. The major soil photolysis products in soil were CGA 339833 (9.1% AR), CGA 192155 (11.7%) and CGA 265378 (12.3%) which reached maximum levels after ca 19 days of natural sunlight.

For the water phase, a water/sediment study has been performed, i.e. Gonzalez-Valero, J., (1992). Degradation in the whole system is recorded and is 451 and 699 days (855 and 1326 days at 12 °C). Degradation values for the water and sediment phase have not been recorded separately. Also no degradation studies have been performed for water and sediment phase separately. Based on the degradation values for the whole system, fludioxonil is fulfilling the **P and vP criteria.**

For the soil phase, laboratory studies have been performed, where primary degradation is recorded. DT50 values ranges from 143 to 482 days (geomean of 265 days, n= 8, 20 °C). DT50 is equal to 502 days at 12 °C (corrected via the Arrhenius equation). Based on the soil degradation half-lives, fludioxonil is fulfilling the **P and vP criteria.**

Photo degradation products: CGA 339833 (formed in water at max. 30.5% AR and in soil at max 9.1% AR), CGA 344623 (formed in water at max. 12.4% AR), A5 (formed in water at max. 11.5% AR) CGA 192155 (formed in soil at max. 11.7% AR) CGA 265378 (formed in soil at max. 12.3% AR)

For the soil phase experimental DT50 values ranges from 9.3 to 16 days (highest value is 16 days, 20 °C), DT50 = 30 days at 12 °C (corrected via Arrhenius equation) for CGA 339833. For CGA 192155 experimental DT50 values in soil ranges from 16 to 24 days (highest value is 24 days, 20 °C), DT50 = 46 days at 12 °C (corrected via Arrhenius equation). For CGA 339833 a hydrolysis half-life of 597 days is found at pH 7 at 25 °C. For the other photo degradation products no experimental data are available. By using the PBT-profiler[6] QSAR degradation half-lives are estimated for the water, soil, sediment and air compartment (see Table below).

Based on the soil degradation studies, CGA339833 and CGA 192155 seems to degrade rather fast. However experimental data are only available for one compartment and as the QSAR estimates are so high for sediment then both of them are considered as **P and vP as well**. For the other photo-degradation products no experimental data are available. For these substances QSAR sediment half-lives are above the triggers of 120 and 180 days and therefore CGA 344623, A5 and CGA 265378 are considered as **P and vP as well.**

6 Developed by the Environmental Health Analysis Center under contract to the Office of Chemical Safety and Pollution Prevention and U.S. Environmental Protection Agency. http://www.pbtprofiler.net/

	QSAR estimates via PBT-profiler[1]			
Substance	**DT50 water (days)**	**DT50 soil (days)**	**DT50 sediment (days)**	**DT50 air (days)**
Fludioxonil	60	120 (Experimental value: 502 days at 12 °C)	540	0.28
CGA 339833	60	120 (Experimental value: 30 days at 12 °C)	540	0.39
CGA 344623	38	75	340	0.34
A5	38	75	340	0.34
CGA 192155	38	75 (Experimental value: 46 days at 12 °C)	340	2.2
CGA 265378	60	120	540	0.75

[1] Developed by the Environmental Health Analysis Center under contract to the Office of Chemical Safety and Pollution Prevention and U.S. Environmental Protection Agency. http://www.pbtprofiler.net/. Estimates are calculated based on input from BIOWIN v4.10

Assessment

P Criteria	**Assessment**
T1/2 > 60 days in seawater, or	Fludioxonil: No experimental data CGA 339833, CGA 344623, A5, CGA 265378 and CGA 192155: No experimental data
T1/2 > 40 days in fresh- or estuarine water, or	Fludioxonil: Data from the water/sediment study are available for the whole system and based on these degradation values (855 and 1326 days at 12 °C) fludioxonil fulfils the P criteria. CGA 339833, CGA 344623, A5, CGA 265378 and CGA 192155: No experimental data
T1/2 > 180 days in seawater sediment, or	Fludioxonil: No experimental data CGA 339833, CGA 344623, A5, CGA 265378 and CGA 192155: No experimental data
T1/2 > 120 days in freshwater- or estuarine sediment, or	Fludioxonil: Data from the water/sediment study are non conclusive regarding degradation in the sediment phase CGA 339833, CGA 344623, A5, CGA 265378 and CGA 192155: No experimental data
T1/2 >= 120 days in soil.	Fludioxonil: In soil a geomean half-life is calculated to 265 days at 20 °C (502 days at 12°C). The P criteria is therefore fulfilled. CGA 192155: In soil the highest half-life is 24 days at 20 °C (46 days at 12°C). The P criteria is not fulfilled. CGA 339833: In soil the highest half-life is 16 days at 20 °C (30 days at 12°C). The P criteria is not fulfilled. CGA 344623, A5 and CGA 265378: No experimental data

vP Criteria	**Assessment**
T1/2 > 60 days in sea-, fresh- or estuarine water water, or	Fludioxonil: Data from the water/sediment study are available for the whole system and based on these degradation values (855 and 1326 days at 12 °C) fludioxonil fulfils the vP criteria.
T1/2 > 180 days in seawater-	Fludioxonil: Data from the water/sediment study are non

vP Criteria	Assessment
, freshwater- or estuarine sediment, or	conclusive regarding degradation in the sediment phase
T1/2 > 180 days in soil.	Fludioxonil: In soil a geomean half-life is calculated to 265 days at 20 °C (502 days at 12°C). The vP criteria is therefore fulfilled

Conclusion on P / vP properties	Fludioxonil is fulfilling the P and vP criterias. CGA 339833, CGA 344623, A5, CGA 265378 and CGA 192155 are fulfilling the P and vP criterias based on QSAR estimates for sediment.

Assessment of bioaccumulation

Screening

Fludioxonil

The experimentally derived BCF_{fish} value considered in the risk assessment is 366 L/kg wet fish based on the whole fish ([redacted]., 1994). A $BCF_{earthworm}$ has been calculated to 159 L/kg wet earthworm.

Fludioxonil has a log Kow of 4.12 (experimental: flask method). A log Koa value has been estimated to 11.783 using KOAWIN v1.10. According to Kelly et al. (2004), substances having low log Kow values (~2 to 5) and high log Koa values (~6 to 12) have a low bioaccumulation potential in aquatic organisms but a high bioaccumulation potential in air-breathing organisms, unless they are rapidly metabolised. Studies in rats show that fludioxonil seems to be rapidly metabolised and it has a low potential for accumulation. Further the volatilisation of fludioxonil to the atmosphere is unlikely to be significant because of its low vapour pressure and, additionally, that any fludioxonil that does enter the atmosphere is expected to undergo rapid photochemical oxidation. However, information on the potential of accumulation in other air-breating organisms (such as reptiles or insects) is not available.

As a conclusion, based upon the BCF values of 366 L/kg wet fish and 159 L/kg wet earthworm (<2000 L/kg) fludioxonil is not considered as bioaccumulative (B) or very bioaccumulative (vB). Additionally, it is not likely that fludioxonil has potential for bioaccumulation in air breathing organisms (other than mammals) as the BCF values indicates that fludioxonil metabolises rapidly.

Photo degradation products: CGA 339833 (formed in water at max. 30.5% AR and in soil at max 9.1% AR), CGA 344623 (formed in water at max. 12.4% AR), A5 (formed in water at max. 11.5% AR) CGA 192155 (formed in soil at max. 11.7% AR) CGA 265378 (formed in soil at max. 12.3% AR)

For all the photo degradation products log Kow estimates are below 4.5 and estimated BCF values (see Table below) are far below the trigger of 2000 L/kg so the substances are not considered bioaccumulative (B) nor very bioaccumulative (vB). As the photo degradation products have structural similarity to fludioxonil it is expected that the mechanism of bioaccumulation for the photo degradation products follow fludioxonil and that the estimated BCF values are reliable.

Substance	log Kow (KOWWIN v1.68)	log Koa (KOAWIN v1.10)	BCF (BCFBAF using log Kow) L/kg wet-wt
Fludioxonil	4.12 (Experimental: flask method)	12	366 (whole fish, experimental) 243 (QSAR estimate based on experimental log Kow)

CGA 339833	1.68	17	3.2
CGA 344623	0.93	19	3.2
A5	3.00 (isomer 1) 2.50 (isomer 2)	14	3.2
CGA 192155	3.17	11	3.0
CGA 265378	3.58	17	110

Assessment

B Criteria	**Assessment**
BCF > 2000	Fludioxonil: The B criteria is not fulfilled as BCF values of 366 L/kg wet fish and 159 L/kg wet earthworm are below 2000 L/kg CGA 339833, CGA 344623, A5, CGA 265378 and CGA 192155: The B criteria is not fulfilled as BCF values are below 2000 L/kg

vB Criteria	**Assessment**
BCF > 5000	Fludioxonil: The vB criteria is not fulfilled as BCF values of 366 L/kg wet fish and 159 L/kg wet earthworm are below 5000 L/kg CGA 339833, CGA 344623, A5, CGA 265378 and CGA 192155: The vB criteria is not fulfilled as BCF values are below 5000 L/kg

Conclusion on B / vB properties	Fludioxonil and the major photo degradion products are not considered as bioaccumulative (B) or very bioaccumulative (vB)

Assessment of toxicity

Screening

Fludioxonil
Based on the chronic ecotoxicology data on Daphnia magna, NOEC (21 days, reproduction) = 0.019 and 0.035 mg/L and on fish, NOEC (28 days, early life stages) = 0.039 mg/L, fludioxonil does not fulfill the toxic (T) categorisation. Fludioxonil does not meet the criteria for classification as carcinogenic, mutagenic or toxic for reproduction according to the CLP Regulation.

As a conclusion, fludioxonil is not considered as toxic (T).

Photo degradation products: CGA 339833 (formed in water at max. 30.5% AR and in soil at max 9.1% AR), CGA 344623 (formed in water at max. 12.4% AR), A5 (formed in water at max. 11.5% AR) CGA 192155 (formed in soil at max. 11.7% AR) CGA 265378 (formed in soil at max. 12.3% AR)

It is not possible with the available information to derive a conclusive decision for the T criterion for the photo degradation products. No chronic nor any acute toxicity studies are submitted for any of the substances. QSAR models have been applied by use of Ecosar v1.11, however these are not applicable for a definitive assessment of the T criterion as stated in the Guidance on information requirements and chemical safety assessment – Chapter R.11: PBT Assessment. None of the QSAR estimates (see Table below) suggest that the photo degradation products fulfil the screening criteria for T. However the estimated chronic values are ChV which represent the geometric mean of NOEC and LOEC. It would therefore be expected that NOEC values are somewhat lower than the chronic values (ChV) given.

Summary table – QSAR estimates for aquatic toxicity							
Organism, endpoint	**Fludioxonil**		**CGA 339833**	**CGA 344623**	**A5 (2 isomers)**	**CGA 192155**	**CGA 265378**
	Experimental data[1] (mg/L)	**QSAR estimate[2] (mg/L)**					
Fish, 96h LC50	0.23	0.14	448	1837	28	2.0	16
Daphnid, 48h LC50	0.40	0.28	59	132	11	0.61	11
Green algae, 96h EC50	0.21 (48h)	0.44	8.4	13	12	0.22	7.4
Fish, ChV[3]	0.039 (NOEC)	0.101	0.32	16	2.6	0.012	1.5
Daphnid, ChV[3]	0.019 (NOEC)	0.000834	4.7	9.8	0.97	0.026	0.64
Green Algae, ChV[3]	0.027 (NOEC)	0.246	5.2	5.0	5.1	0.327	3.3

1: lowest value

2: lowest value estimated by Ecosar v1.11

3: ChV - Chronic value is defined as the geometric mean of the no observed effect concentration (NOEC) and the lowest effect concentration (LOEC). This can be mathematically represented as: ChV=10^(log(LOEC x NOEC)/2)

Assessment

T Criteria	Assessment
NOEC/EC10 (long-term) < 0.01 mg/L for freshwater or seawater organisms, or	Fludioxonil: The T criterion is not fulfilled as the NOEC values are above the trigger of 0.01 mg/L CGA 339833, CGA 344623, A5, CGA 265378 and CGA 192155: None of the QSAR estimates of ChV are below the trigger of 0.01 mg/L.
substance meets the criteria for classification as carcinogenic (category 1A or 1B), germ cell mutagenic (category 1A or 1B), or toxic for reproduction (category 1A, 1B or 2) according to the CLP Regulation, or	Fludioxonil does not meet any of these criteria
there is other evidence of chronic toxicity, as identified by the substance meeting the criteria for classification:specific target organ toxicity after repeated exposure (STOT RE category 1 or 2) according to the CLP Regulation.	Fludioxonil does not meet any of these criteria

Conclusion on T properties	Fludioxonil does not fulfill the T criterion. There are no conclusive data on if the photo-degradation products fulfil the T criteria. None of the QSAR estimates of ChV are below the trigger of 0.01 mg/L.

Summary and overall conclusions on PBT or vPvB properties

Overall conclusion:
Based on the assessment described in the subsections above the submission substance is not a PBT / vPvB substance, however fludioxonil fulfils the criteria for being vP. The photo-degradation products are vP based on QSAR estimates.

5.2 SUBSTITUTION CRITERIA

The table below summarises the relevant information with respect to the assessment of the substitution criteria:

Substitution criteria (BPR, Article 10)	**Assessment**
One of the exclusion criteria listed in Article 5(1) is met but AS may be approved in accordance with Article 5(2)	The exclusion criteria listed in Article 5(1) is not met
The criteria to be classified, in accordance with Regulation (EC) No 1272/2008, as a respiratory sensitiser is met	Fludioxonil does not meet any of these criteria (no data)
The acceptable daily intake, acute reference dose or acceptable operator	-

Substitution criteria (BPR, Article 10)	**Assessment**
exposure level, as appropriate, is significantly lower than those of the majority of approved active substances for the same product-type and use scenario	
Two of the criteria for being PBT in accordance with Annex XIII to Regulation (EC) No 1907/2006 are met	Fludioxonil meets the vP categorisation
There are reasons for concern linked to the nature of the critical effects which, in combination with the use patterns, amount to use that could still cause concern, such as high potential of risk to groundwater, even with very restrictive risk management measures	There are no concerns related to critical effects
The AS contains a significant proportion of non-active isomers or impurities.	There is no significant content of non-active isomers or impurities in the AS

Conclusion on substitution criteria	Fludioxonil does not meet the conditions laid down in Article 10 of Regulation (EU) No 528/2012.

5.3 ASSESSMENT OF LONG-RANGE ENVIRONMENTAL TRANSPORTATION AND IMPACT ON ENVIRONMENTAL COMPARTMENTS

	Assessment
The active substance or a degradation product is a persistent organic pollutant (POP) listed in Annex I of EC 850/2004	Neither fludioxonil nor the degradation products are listed as persistent organic pollutants
Assessment of long-range transport potential (LRTAP): • Vapour pressure <1000 Pa and • half-life in air > 2 days or • Monitoring data in remote area showing that the substance is found in remote regions or • Result of multi media modelling	There is no concern regarding long-range transport potential of fludioxonil. The vapour pressure of fludioxonil is 3.9 x 10^{-7} Pa at 25 °C (below 1000 Pa) and the half-life in air is 6.7 hours (below 2 days). There are no monitoring data showing that the substance is found in remote regions. All the photo-degradation products have estimated vapour pressures below 1000 Pa. Estimated half-life in air is just above 2 days (2.2 days) for CGA 192155, while for the other photo-degradation products half-lifes are below 2 days. No monitoring data for remote regions are available for the substances.
The active substance or a degradation product is vP/vB or T?	Fludioxonil meets the vP criteria. The photo-degradation products are vP based on QSAR estimates.

Conclusion on LRTAP/POP asessment	Fludioxonil fulfils the criteria for being vP. However fludioxonil does not demonstrate the potential for long range transport. In view of this, fludioxonil does not meet the criteria for being a persistent organic pollutant. The photo-degradation products are vP based on QSAR estimates. None of the substances demonstrate potential for long range transport. The substances do therefore not fulfil the criteria for being persistent organic pollutants.

Part B Exposure assessment and effects of the active substance in the biocidal product(s)

6 GENERAL PRODUCT INFORMATION

6.1 IDENTIFICATION OF THE PRODUCT

Name(s) of the product	
Trade name(s) or proposed Trade name(s)	Sporgard WB
Manufacturer's development code and number of the product	[redacted]
Formulation type	Aqueous dispersion

6.2 COMPLETE QUALITATIVE AND QUANTITATIVE COMPOSITION OF THE BIOCIDAL PRODUCT

Active substance(s)					
ISO or Trivial name	**IUPAC name or other accepted chemical name**	**EC number**	**CAS number**	**Composition / all constituents (upper and lower concentration limit in % (w/w))#**	**Concentration in the product in % (w/w)**
Fludioxonil	4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1H-pyrrole-3-carbonitrile	-	131341-86-1	95 % (w/w)	1.96
Thiabendazole*	4-(1H-1,3-benzodiazol-2-yl)-1,3-thiazole	-	148-79-8	-	19.1
Azoxystrobin*	Methyl (2E)-2-(2-{[6-(2-cyanophenoxy)pyrimidin-4-yl]oxy}phenyl)-3-methoxyacrylate	-	131860-33-8	-	19.8

*For the current evaluation only fludioxonil is considered.
#Information on the impurities of fludioxynil is confidential and can be found in IUCLID section 2.9. Furthermore information regarding Thiabendazole and Azoxystrobin can be found under the respective substances in section 2.9 and 13 in IUCLID.

Other components / ingredients of the product					
ISO or Trivial	**IUPAC**	**EC number**	**CAS number**	**Concentration in**	**Function**

name	**name or other accepted chemical name**			**in the product in % (w/w)**	

The composition of Sporgard WB is confidential. Please see IUCLID section 2.3 for information on the composition of the product.

6.3 PHYSICAL, CHEMICAL AND TECHNICAL PROPERTIES

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Physical state at 20°C and 101.3 kPa	Liquid	EPA OPPTS 830.6303 (Physical State)	-	Irrig, H., 2007 (IUCLID 3.1-01)
Colour at 20°C and 101.3 kPa	Yellow	EPA OPPTS 830.6302 (Color)	-	Irrig, H., 2007 (IUCLID 3.1-01)
Odour at 20°C and 101.3 kPa	Faintly aromatic odour	EPA OPPTS 830.6304 (Odour)	-	Irrig, H., 2007 (IUCLID 3.1-01)
Acidity / alkalinity	pH 6.5	CIPAC MT 75.3	Determined in a 1% solution in deionised water at a temperature of 25 °C	Irrig, H., 2007 (IUCLID 3.2-01)
	The pH results were within the range 7.11 - 7.28	Equivalent to CIPAC MT 75	The pH of the neat product, a 10% dilution and a 1% dilutions of the product were determined, in duplicate, using a calibrated Mettler Toledo pH meter at approximately 21.5 °C.	Wachtler, P, 2014 (IUCLID 3.2-02)
Relative density	1.187 g/cm3	OECD Guideline 109 (Density of Liquids and Solids)	The density has been determined at 20 °C using an oscillating density meter	Irrig, H., 2007 (IUCLID 3.3-01)
Storage stability, stability and shelf-life				
Accelerated storage	-	-	A long term storage stability test is available which shows that Sporgard WB is stable at 20°C/50% RH. The product is not intended to be stored at temperatures exceeding 30°C and label instructions indicate the product should not be stored at high temperatures. Under these circumstances an accelerated storage test is not considered necessary. The analytical method used for the active substance content determination is validated.	(IUCLID 3.4.1-01)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Long term storage at ambient temperature	The product is chemically stable at ambient temperature for at least one year	EPA OPPTS 830.6320 (Corrosion Characteristics) EPA OPPTS 830.6317	The product Sporgard WB is chemically stable at ambient temperature (20°C, 50% relative humidity) for at least one year in containers made with non-fluorinated HDPE or stainless steel (separate studies). There was no decline in the active substance content after storage for 1 year compared to the initial measurement. There were no physical changes in the container and package materials after storage at 20°C and 50% RH for 1 year, and no physical changes to the containers that would interfere with the proper use of the product. All assay values in the studies through one year are within acceptable limits, 2 and 4 % respectively. Based on the stability data, the product is chemically stable at ambient temperature for at least one year. No data on other physical parameters were investigated in the study and the physical stability of the product could not be determined. Therefore, a gap is identified for this data requirement and data confirming the physical and chemical stability of the product must be submitted at product authorisation level. For further data please see table 6.4-1 The analytical method used for the active substance content determination is validated.	Irrig, H, 2008 (IUCLID 3.4.1-03)
	The product is	LXS TM internal method	A sample of Sporgard WB was stored in the	Bickers, C, 2014 (IUCLID

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
	chemically stable at ambient temperature for at two years		original packaging material (Polyethylene Drum) at ambient temperature (20°C ± 5°C) for 24 months. The content of the active ingredients were determined before storage and after storage by HPLC analysis with UV detection. It is assessed that the product is chemically stable at ambient temperature for two years No data on physical parameters were investigated in the study and the physical stability of the product could not be determined. Therefore, a gap is identified for this data requirement and data confirming the physical and chemical stability of the product must be submitted at product authorisation level. For further data please see table 6.4-2 The analytical method used for the active substance content determination is validated.	3.4.1-04)
Low temperature stability (liquids)	-	-	The product is not intended to be stored at low temperatures and label instructions indicate that storage of the product should avoid frost conditions. Under these circumstances a low temperature stability storage test is not considered necessary.	(IUCLID 3.4.1-02)
Effects on content of the active substance				
Light	-	-	A study does not need to be performed as the product is packaged in opaque material and	(IUCLID 3.4.2.1-01)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
			therefore not exposed to light.	
Temperature and humidity	-	-	A long term storage stability test is summarized in IUCLID 3.4.1-03, this shows Sporgard WB is stable for at least 1 year at 20°C and 50% relative humidity. No decline in active substance concentration was observed over the test period. There were no significant changes to the physical appearance of the product, other than a slight separation of liquid after 6, 9 and 12 months storage which was resolved on mixing. Homogeneity was not affected. There was no significant weight loss in the test samples after storage for 1 year. Based on these existing data, it is not expected that temperature or humidity will significantly affect stability of the active substances or physical characteristics of Sporgard WB. Separate tests at different temperatures and humidity levels are not considered necessary.	(IUCLID 3.4.2.1-02)
Reactivity towards container material	No reactivity observed	EPA OPPTS 830.6320 (Corrosion Characteristics)	There were no changes in the physical appearance of the container and package materials after storage at 20°C and 50% RH for 1 year, and no physical changes to the containers that would interfere with the proper use of the product. Based on the stability data, there is no reactivity of the product towards the container material for at least one year.	Irrig, H, 2008 (IUCLID 3.4.1-05)
Technical characteristics				
Wettability	-	-	Not required for a liquid formulation.	(IUCLID 3.5-02)
Suspensibility, spontaneity and dispersion stability	-	-	Suspensibility and spontaneity are not required for a liquid formulation and as it is not to be diluted.	(IUCLID 3.5-01) and (IUCLID 3.5-02)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
			Sporgard WB is an aqueous dispersion. A long term storage stability test is summarize in IUCLID 3.4.1-03. This shows Sporgard WB is stable for at least 1 year at 20°C and 50% relative humidity. No decline in active substance concentration was observed over the test period. There were no significant changes to the physical appearance of the product, other than a slight separation of liquid after 6, 9 and 12 months storage which was resolved on mixing. Homogeneity was not affected. The available data indicate that the Sporgard WB aqueous dispersion is stable.	
Wet sieve analysis and dry sieve test	-	-	Not required for a liquid formulation.	(IUCLID 3.5-02)
Emulsifiability, reemulsifiability and emulsion stability	-	-	Not required for a liquid formulation.	(IUCLID 3.5-02)
Disintergration time	-	-	Not required for a liquid formulation.	(IUCLID 3.5-02)
Particle size distribution, content of dust / fines, attrition, friability	-	-	Not required for a liquid formulation.	(IUCLID 3.5-02)
Persistent foaming	-	-	The persistent foaming test is not applicable to the product because it is not intended to be diluted with water.	(IUCLID 3.5-02)
Flowability, pourability,	-	-	Not required for a liquid formulation.	(IUCLID 3.5-02)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
dustability				
Burning rate – smoke generators	-	-	Not required for a liquid formulation.	-
Burning completeness – smoke generators	-	-	Not required for a liquid formulation.	-
Composition of smoke – smoke generators	-	-	Not required for a liquid formulation.	-
Spraying pattern - aerosols	-	-	Not required for a liquid formulation.	-
Other technical characteristics	-	-	Not relevant	-
Physical and chemical compatibility with other products including other biocidal products with which its uses is to be authorised				
Physical compatibility	-	-	Sporgard WB is not intended to be use in conjunction with other biocidal products. Sporgard WB can be applied to, or impregnated into; paper, wallboard, gypsum, paperboard, water-based paints and coatings, caulks, sealants, adhesives and textiles. Sporgard WB is an aqueous dispersion that is compatible with these materials.	(IUCLID 3.6-01)
Chemical compatibility	-	-	Sporgard WB has no corrosive or other highly reactive properties that would make it chemically incompatible with these materials.	(IUCLID 3.6-01)
Degree of dissolution and dilution stability	-	-	Not relevant. The product is not intended to be diluted with water.	-

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Surface tension	σ = 40.49 mN/m at 20 °C	OECD Guideline 115 (Surface Tension of Aqueous Solutions). Ring method. DIN EN 14370	An automatic tensiometer (ring method) was used. The sample was dissolved in water (0.1%) and tempered at 20 °C.	Keldenich, H.-P., 2014 (IUCLID 3.8-01)
Viscosity	606 mPaS at 20 °C	EPA OPPTS 830.7100 (Viscosity) using a rotational viscometer	The viscosity was determined with a Brookfield viscometer. Viscosity only tested at 20 °C	Irrig, H., 2007 (IUCLID 3.9-01)
	Thixotropic at 20 °C 106.3 mPa·s at 40 °C	OECD Test Guideline 114 (Viscosity of Liquids) using a rotational viscometer DIN 53019	-	Keldenich, H.-P., 2014 (IUCLID 3.9-02)
Physical hazards and characteristics				
Explosives	The test substance was determined to be non-explosive.	EU Method A.14 (Explosive properties)	The thermal sensitivity and mechanical sensitivity (shock) were tested	Irrig, H., 2007 (IUCLID 4.1-01)
Flammable gases	-	-	Not required for a liquid formulation.	-
Flammable aerosols	-	-	Not required for a liquid formulation.	-
Oxidising gases	-	-	Not required for a liquid formulation.	-
Gases under pressure	-	-	Not required for a liquid formulation.	-
Flammable liquids	No flash point up to the boiling point (100 °C).	EU Method A9	The test was carried out in accordance with EC test A9 using the Pensky-Marten closed cup testing. No flash point was detected below 100°C, the onset of boiling. The test substance is not classified as flammable in terms of its flash point.	Irrig, H., 2007 (IUCLID 4.2-01)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
Flammable solids	-	-	Not required for a liquid formulation.	-
Self-reactive substances and mixtures	Sporgard WB is not regarded as a self-reactive substance or mixture.	-	Sporgard WB contains no substance that is classified for physical chemical hazard and no substance that by its chemical nature would indicate the potential for self-reaction.	(IUCLID 4.17-02)
Pyrophoric liquids	Sporgard WB is not regarded as a pyrophoric liquid.	-	Sporgard WB contains no substance that is classified for physical chemical hazard and no substance that by its chemical nature would indicate the potential for Pyrophoric behaviour.	(IUCLID 4.17-03)
Pyrophoric solids	-	-	Not required for a liquid formulation.	-
Substances and mixtures which in contact with water emit flammable gases	Sporgard WB does not emit flammable gases in contact with water.	-	Sporgard WB is a stable aqueous formulation that does not emit flammable gases in contact with water.	(IUCLID 4.17-05)
Oxidising liquids	The test substance is not classified as an oxidising substance	UN Test O.2	The test was carried our in accordance with UN Test O.2, 'Test for Oxidising Liquids.' The test mixture produced pressure rises which were above the 4.2 seconds average for the 65% aqueous nitric acid/cellulose reference mixtures. In accordance with the criteria of UN Test O.2, the test substance is not classified as an oxidising substance.	Irrig, H., 2007 (IUCLID 4.4-01)
Oxidising solids	-	-	Not required for a liquid formulation.	-
Organic peroxides	-	-	Not applicable, the product contains no organic peroxides.	(IUCLID 4.17-06)
Corrosive metals	'Sporgard WB' is not corrosive to steel and not corrosive to	Recommendations on the Transport of Dangerous Goods – Manual of Tests and	UN test specifications require metal plates of dimension (LxWxT) 50 x 20 x 2 mm. In the test metal plates of 50 mm length, 15 mm	Keldenich, H.-P., 2014 (IUCLID 4.17-07)

Property	Result	Test method applied or description in case of deviation	Remarks / Discussion / Justification for waiving	References
	aluminum.	Criteria' (fifth revised edition, 2009) section 37.4 ,Test methods for corrosion to metals' Test C.1	width and 3 mm thickness (steel) or 5 mm thickness (aluminum), respectively, were used. According to UN 37.4 (C.1 Test), corrosion rate of the test item 'Sporgard WB' with steel or with aluminum is < 6.25 mm/year. No pitting corrosion was observed by visual inspection (observed syncline was caused by cold deformation). After the corrosion test the steel sample in the test item showed abnormalities at the surface and three synclinal points were observed. In order to determine whether these local indications are pitting corrosion, at the optically deepest spot, a metallographic microsection was made across this point. Below the synclinal surface characteristics of cold deformation were seen. The depth is about 30 µm. Since features of cold deformation have been found in the structure, the most probable reason for these synclines is purely mechanical (e.g. by particles pushed into the surface during rolling) and pitting corrosion can be excluded.	
Auto-ignition temperature of products (liquid and gas)	'Sporgard WB' has no auto ignition temperature up to 600 °C at 1008 hPa.	EU Method A.15 (Auto-Ignition Temperature (Liquids and Gases)) DIN 51794	The auto ignition temperature of 'Sporgard WB' was tested according to EC Test Procedure A 15. 'Sporgard WB' had no auto ignition temperature up to 600 °C at 1008 hPa.	Keldenich, H.-P., 2014 (IUCLID 4.17.1-01)
Relative self-igniton temperature of solids	-	-	Not applicable, Sporgard WB is a liquid formulation.	-
Dust explosion hazard	-	-	Not applicable, Sporgard WB is a liquid formulation.	-

6.4 HAZARD IDENTIFICATION FOR PHYSICAL AND CHEMICAL PROPERTIES

Sporgard WB is a yellow, faintly aromatic, moderately viscous liquid. Tests have shown Sporgard WB not to be explosive, oxidising or flammable and as such the product will not require labelling for physical chemical hazard. Sporgard WB has a pH of 6.5 and is chemically and physically stable when stored at 20°C and 50% relative humidity and has no reaction with stainless steel or non-fluorinated HDPE containers. The product shelf-life is expected to be at least 2 years.

Storage stability

Accelerated storage stability

A waiver was submitted for the accelerated storage stability study, which is acceptable as the long-term study for the product has been submitted, and as the accelerated study will be required at the product authorization level.

Long-term storage stability

1 year data (Irrig, 2008)

The stability of the product Sporgard WB in non-fluorinated HDPE and stainless steel packaging was assessed following storage at ambient temperature for one year.

The % active ingredient was measured and the package/container visually evaulated before and after storage.

The samples were analysed for the active ingredients using HPLC-UV.

There was only a slight variation in the active substance content during storage for 1 year compared to the initial measurement in both HDPE and stainless steel, which is considered acceptable. Please see table of results below.

Table 6.4-1: Storage stability - variation in active substance contents (Irrig, 2008)

Packaging	HDPE	Stainless Steel
Time point	% Fludioxonil	
0 months	2.02	2.02
3 months	1.99	2.00
6 months	2.02	2.04
9 months	2.10	2.06
12 months	1.99	1.99
Max change (%)	4	2

The weights of the test system samples were monitored and showed no significant changes from initial values.

Visual examination of the corrosion sample indicated no physical changes in the test container/package after 1 year of storage.

Conclusion:

The product Sporgard WB is chemically stable at ambient temperature (20°C, 50% relative humidity) for at least one year in containers made with non-fluorinated HDPE or stainless steel (separate studies). There was no decline in the active substance content after storage for 1 year compared to the initial

measurement. There were no physical changes in the container and package materials after storage at 20°C and 50% RH for 1 year, and no physical changes to the containers that would interfere with the proper use of the product.
No data on other physical parameters were investigated in the study and the physical stability of the product could not be determined. Therefore, a gap is identified for this data requirement and data confirming the physical and chemical stability of the product must be submitted at product authorisation level.

2 year data (Bickers, 2014)

A sample of Sporgard WB was stored in the original packaging material at ambient temperature (20°C ± 5°C) for 24 months. The content of the active ingredients were determined before storage and after storage by HPLC analysis with UV detection.

PACKAGING
- Type of container / packaging: polyethylene drums
- Pack size: 200 kg drums
- Approximate empty weight or volume: 10.16 kg

TEST CONDITIONS
- Study duration: 2 years
- Temperature: 20°C ± 5°C
- Humidity: not recorded
- Sampling times: immediately after manufacture and (19 Oct 2011) and then after 2 years storage (30 Oct 2013)

ANALYTICAL METHODS
- Analytical method used: HPLC-method with UV detection at 265 nm
- Handling of test samples prior to sampling: not recorded

The content of the active ingredients were determined before storage and after storage by HPLC analysis with UV detection. There was no change in concentration of the active substance in the formulated product after 2 years storage in the 200kg drum at ambient temperature in a warehouse. The product can be considered to be stable for at least 24 months.

No data on physical parameters were investigated in the study and the physical stability of the product could not be determined. Therefore, a gap is identified for this data requirement and data confirming the physical and chemical stability of the product must be submitted at product authorisation level.

Table 6.4-2: Storage stability - variation in active substance contents (Bickers, 2014)

Sporgard WB **Batch:** [redacted]	**Start value (date: 2011-10-19)**	**2 year storage at ambient temperature** **(date:2013-10-30)**
Fludioxonil	**1.84 %**	**1.84 %**

6.5 ANALYTICAL METHODS FOR DETECTION AND IDENTIFICATION

Analytical methods for the analysis of the product as such including the active substance, impurities and residues									
Analyte (type of analyte e.g. active substance)	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**	**Recovery rate (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
					Range	Mean	RSD		
Fludioxonil	RP HPLC-UV 220 nm	Accuracy measured at 80%, 100% and 120% of the expected concentration on duplicate samples Linearity measured at 75%, 100% and 125%	r^2 = 0.9998	There were no interfering substances ≥ 3%, relative to the analyte	98.2 to 101.9%	100.1%	0.46 % based on 6 repli-cates	LOQ are not required for formulations containing high con-centrations of active substances (≥ 1% w/w)	Johnson, A., 2007 (IUCLID 5.1-01)

Only fludioxonil is considered in the summary of the analytical methods for the analysis of the product in this dossier as the two other active substances azoxystrobin and thiabendazole are evaluated in other CARs. Further information regarding Thiabendazole and Azoxystrobin can be found under the respective substances in section 5.1-01 in IUCLID.

Summary of analytical method

Accuracy was measured by analyzing the mixture containing fludioxonil at 80%, 100% and 120% of the expected concentration for each active substance. Duplicate samples were prepared and analysed on a single occasion. The recovery results are the following:

Fludioxonil - 98.2 to 101.9%

The recovery results for fludioxonil are between 97 and 103% which is considered acceptable for an active substance concentration between 1 and 10%. The method is therefore considered to be accurate for the active substance.

Limit of quantitation (LOQ): Measurement of LOD and LOQ are not required for formulations containing high concentrations of active substances (≥ 1% w/w).

Precision: The relative standard deviation from 6 replicates was calculated as:

Fludioxonil - %RSD = 0.46 The relative standard deviation is significantly lower than the suggested criteria for an analyte at approximately 1% concentration and the method is therefore considered to be precise

Reliability of method: It is not expected that analysis of the Sporgard WB formulation will be conducted in laboratories other than those operated by the formulation manufacturer (Lanxess).

Linearity was tested using 3 concentrations of fludioxonil in the range of 75%, 100% and 125% of the expected substance concentration range.The coefficient of variation for the active substance is: Fludioxonil r2 = 0.9998. The coefficient of variation result is > 0.999 and therefore the method is considered to be linear over the concentration range tested.

Specificity was confirmed by analyzing blank Sporgard WB formulation (without active substance). There were no interfering substances ≥ 3%, relative to the analyte. The method is based on HPLC which is considered to be a selective analytical method.
The method is considered to be specific for fludioxonil.

The method is based on commonly used analytical methods and equipment, and involves detection of the analyte by UV absorption. The method is considered to be robust based on the simple analytical techniques employed.

The determination of the active substance, fludioxonil, was carried out using HPLC on a reversed phase C18 column using a linear gradient program and UV detection at 220 nm. Quantification was achieved by comparison of peak area with an external standard.

The method for identification of the active substance has been adequately validated and meets the EU criteria with respect to specificity, linearity, accuracy and precision as described in the ECHA guidance document 2014.

The method is considered sufficiently robust for use in assessing the fludioxonil content of Sporgard WB. The method requires equipment and instrumentation which is commonly available in most well-equipped laboratories. Therefore, the method is suitable for enforcement purposes.

Analytical methods for monitoring

In the scope of this dossier, the toxicologically and ecotoxicologically relevant compound in the biocidal product Sporgard WB is fludioxonil. The two other active substances azoxystrobin and thiabendazole are evaluated in other CARs. Further information regarding Thiabendazole and Azoxystrobin can be found under the respective substances in section 5.2-01 and 5.3-01 in IUCLID. Methods for the determination of fludioxonil in soil, water and air are presented in the active substance dossier and are considered adequate since the co-formulants in Sporgard WB will not influence the behaviour of fludioxonil should it be released into the environment. Methods for the determination of fludioxonil in animal and human body fluids and tissues, and treated food or feedingstuffs are not considered necessary. The active substance is not classified as toxic or highly toxic and the product is not intended to come into contact with food or feedingstuffs. Further methods specific to Sporgard WB are not considered necessary.

7 EFFICACY

7.1 EFFICACY

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
Fungicide	Material preservation in PT 7.	Styrene paint formulated at a range of fungicide concentration of Sporgard - 1500 to 16000 ppm. Paint was commercial product from Sherwin Williams – styrene emulsion paint based on styrene & acrylic co-polymers. Coats of paint (x3) were applied to filter papers (both sides), dried, sterilised by UV and tested	ASTM G-21. Strains used: *Aspergillus niger, Penicillium pinophilum, Chaetomium globosum Gliocladium virens, Aureobasidium pullulans* ASTM D-5590. Strains used: *Aspergillus niger, Penicillium pinophilum, Aureobasidium pullulans* DIN EN 15457. Strains used: *Aspergillus niger, Penicillium purpurogenum, Cladosporium cladosporioides, Aureobasidium pullulans*	Antifungal test metods: ASTM G-21, ASTM D-5590 and DIN EN 15457 ASTM G-21 Determining Resistance of Synthetic Polymeric Materials to Fungi ASTM D-5590 Standard Test Method for Determining the Resistance of Paint Films and Related Coatings to Fungal Defacement by Accelerated Four Week Agar Plate Assay DIN EN 15457 Laboratory Method for testing the Efficacy of Film Preservatives in a Coating against Fungi.	Samples were examined for fungal growth growth on days 7, 14, 21 and 28 (with the exception of test DIN 15457 which completed on day 21).	The results show that Sporgard can resist fungal growth for at least 4 weeks in the standard methods at a minimum concentration of 1500 to 4000 ppm (0.15 to 0.4%) in styrene paint. The minimum effective concentration is consistent with the intended Sporgard dose rate in paint (0.15 to 1.6%).	Twaddle, 2012a IUCLID 6.7-01

Fungicide	Material preservation in PT 7.	Vinyl acrylic paint formulated at a range of fungicide concentration of Sporgard - 1500 to 16000 ppm.	The same strains for the methods ASTM G-21, ASTM D-5590 and DIN EN 15457 as stated above.	Antifungal test methods: ASTM G-21, ASTM D-5590 and DIN EN 15457.	Samples were examined for fungal growth growth on days 7, 14, 21 and 28 (with the exception of test DIN 15457 which completed on day 21).	The results show that Sporgard can resist fungal growth for at least 4 weeks in the standard methods at a minimum concentration of 1500 to 3000 ppm (0.15 to 0.3%) in acrylic vinyl paint. The minimum effective concentration is consistent with the intended Sporgard dose rate in paint (0.15 to 1.6%).	Twaddle. 2012b IUCLID 6.7-02
Fungicide	Material preservation in PT 10.	Industrially produced gypsum board gypsum board samples prepared by the manufacturer containing different concentrations of Sporgard WB (0.025%, 0.05%, 0.075% and 0.1%).	*Aspergillus niger, Penicillium pinophilum, Chaetomium globosum Gliocladium virens, Aureobasidium pullulans*	ASTM G-21: Standard Practice for Derminig Resistance of Synthetic Polymeric Materials to Fungi.	Samples were assessed visually according to the ASTM G 21-96 assessment system.	The results show that Sporgard WB can resist fungal growth of the standard ASTM G 21 strains in gypsum board at a minimum concentration of 0.05%. The minimum effective concentration is consistent with the intended Sporgard dose rate in gypsum board.	Herbertz, 2012a IUCLID 6.7-03
Fungicide	Material	Paper samples	*Aspergillus niger,*	ASTM G-21:	Samples were	The results show	Herbertz, 2012b

	preservation in PT 9.	(green cardboard, 170-190g/m^2 quality) were prepared by the manufacturer containing different concentrations of Sporgard WB (0.15%, 0.25%, 0.35%, 0.45% and 0.55%).	*Penicillium pinophilum, Chaetomium globosum Gliocladium virens, Aureobasidium pullulans, Stachybotrys chartarum*	Standard Practice for Derminig Resistance of Synthetic Polymeric Materials to Fungi	assessed visually according to the ASTM G 21 system.	that Sporgard WB on paper can prevent growth of the standard ASTM G 21 fungi strains at 0.25%, but to resist growth of *Stachybotrys chartarum* a concentration of 0.45% was required. 0.25% is consistent with the intended Sporgard minimum dose rate range in paper, although the dose rate is likely to give poor control. However, the maximum intended concentration of 0.5 % will give good control of all the fungi strains tested.	IUCLID 6.7-04
Fungicide	Material preservation in PT 7.	Industrially produced mineral sealant / grout powder product, was used (pH of wet grout was 11). Grout was prepared with varying amounts	*Aspergillus niger, Penicillium pinophilum, Chaetomium globosum Gliocladium virens, Aureobasidium pullulans*	ASTM G-21: Standard Practice for Derminig Resistance of Synthetic Polymeric Materials to Fungi.	Samples were assessed visuallyaccording to the ASTM G 21-96 assessment system.	The results show that Sporgard WB can resist fungal growth of the standard ASTM G 21 strains in mineral sealant/grout at a concentration of	Herbertz, 2013 IUCLID 6.7-05

		of Sporgard WB (0.025%, 0.05%, 0.1% and 0.15%). Speciments prepared and dried for 24 hours. As a pre-treatment before microbiological testing, the test samples were stored for 4 weeks in a CO_2 atmosphere.				0.05%, 0.1% and 0.15%. The minimum effective concentration is consistent with the intended Sporgard dose rate in mineral sealant / grout powder.	
Fungicide	Material preservation in PT 7, 9 and 10.	Sporgard WB containing 19% Thiabendazole, 19% Azoxystrobin and 1.9% Fludioxonil.	*Alternaria alternata, Aspergillus niger, Aspergillus versicolor, Aureobasidium pullulans, Chartomium globosum, Cladosporium cladosporioides, Cladosporium sphaerospermum, Gliocladium virens, Penicillium brevicompactum, Penicillium chrysogenum, Penicillium citrinum, Penicillium funicolosum, Penicillium glaucum, Penicillium pinophillum,*	Test was performed according to internal methods of the test laboratory which were attached to the original report M 2 02-00012-12. Microbial growth in test wells is compared to microbial growth of the positive controls.	The concentration of test substance fludioxonil at which fungal growth can no longer be detected was determined and is stated as the minimum inhibitory concentration (MIC). The MIC values are given in ppm. The following concentrations were tested: 0, 1, 5, 10, 20, 30, 40, 50, 75, 100, 250, 500 ppm, respectively.	The MIC (minimum inhibitory concentration) values of Sporgard WB against almost all of the tested fungi wre in the range between 5 pm and 35 ppm. Against *Aspergillus niger* Sporgard WB only showed moderate efficacy (MIC value: 250 ppm)	Gerharz, 2014; Rierhausen, 2009; Rech, 2013 IUCLID 6.7-06; 6.7-07; 6.7-08

			Stachybotrys chartarum,				
Fungicide	Material preservation in PT 7, 9 and 10.	Sporgard WB original containing 19% Thiabendazole, 19% Azoxystrobin and 1.9% Fludioxonil compared to Sporgard WB modified containing 1.9% Fludioxonil as a stand-alone active substance.	*Alternaria alternata, Aspergillus niger, Aspergillus versicolor, Aureobasidium pullulans, Chartomium globosum, Cladosporium cladosporioides, Fusarium solani, Paecilomyces variotii, Penicillium chrysogenum, Penicillium funicolosum, Penicillium pinophillum, Scopulariopsis brevicaulis, Sydowia pythiophila, Stachybotrys chartarum, Trichoderma virens*	Test was performed in accordance with LANXESS internal method no. M 2 02-00012-12E. Microbial growth in test wells is compared to microbial growth of the positive controls.	The concentration of test substance fludioxonil at which fungal growth can no longer be detected was determined and is stated as the minimum inhibitory concentration (MIC). Sporgard WB original and Sporgard WB modified were tested in the concentrations 0-2000 ppm and 0-5000 ppm, respectively. Every concentration was tested in triplicate.	The test results show that Fludioxonil provides innate fungicidal efficacy against the organisms *Alternaria alternata, Aspergillus versicolor, Cladosporium cladosporioides, Penicillium pinophillum, Scopulariopsis brevicaulis, Sydowia pythiophila* and *Stachybotrys chartarum* when formulated stand-alone in a representative biocidal product (MIC values 50-750 ppm). In comparison Sporgard WB original showed fungicidal efficacy against all tested organisms with MIC values. beween 5 and 50 ppm, except for *Aspergillus niger* (MIC value: 500 ppm). In	Rech, 2016 IUCLID 6.7-09

						conclusion the study demonstrates innate fungicidal activity of fludioxonil against specific fungi when formulated as a stand-alone test product. These fungi includes *Alternaria alternata, Aspergillus versicolor, Cladosporium cladosporioides, Penicillium pinophillum, Scopulariopsis brevicaulis, Sydowia pythiophila* and *Stachybotrys chartarum.*	

7.2 MODE OF ACTION

Fludioxonil belongs to the phenylpyrrole class of fungicides (PP-fungicides). The mode of action of fludioxonil is by inhibition of a mitogen-activated protein (MAP) kinase in signal transduction of osmo-regulation (glycerol synthesis). Fludioxonil acts immediately on the target mode of action and there is no time delay for efficacy (Fungicide Resistance Action Committee -2014).[7]

7.3 RESISTANCE

Fludioxonil has a single site mode of action. Fungicides with a single site mode of action are more prone to the development of resistance because any change(s) that might occur in the fungus to alter that single site could render the fungus resistant to the fungicide. The potential for resistance development therefore in principle exists, but is restricted by the manner in which fludioxonil is used in the biocidal product. Typical management strategies for fungicide resistance include; not using sub-lethal application rates that may select for fungicide resistance and applying mixtures of two or more fungicides that have different modes of action.

Fludioxonil is intended for use in the product Sporgard WB which contains a mixture of fungicides that present different modes of action. The fungicide action of Sporgard WB will therefore be multi-site and the possibility of resistance development is considerably reduced. Information presented in Section IIIB 6.7 confirms that Sporgard WB is an effective fungicide in end-use items across a range of concentrations. Sub-lethal effects are therefore unlikely to occur and the potential for resistance is minimised.

7.4 CONCLUSION ON EFFICACY

Fludioxonil is a fungicide not intended to be used as a stand-alone substance, it is intended to be used in combination with other fungicides for indoor material preservation in PT 7, 9 and 10. The efficacy of fludioxonil alone has been shown in Document IIIA Section 6 and Document IIIB Section 6. It provides specific activities against *Alternaria alternata*, *Aspergillus versicolor*, *Stachybotrys chartarum*, *Scopulariopsis brevicaulis,* some *Penicillium* spp., *Alternaria* spp. and some wood decaying fungi, such as *Conophora puteana*, *Gloeophyllum trabeum* and *Sydowia pythiophila*.

Sporgard WB is a preservative biocidal product containing the fungicide active substances fludioxonil, azoxystrobin and thiabendazole. The use of three active substances in Sporgard WB ensures that the product maintains its efficacy by presenting multiple mechanisms of fungicidal activity, thereby minimising the possibility of resistance development.

The product has broad spectrum efficacy, but the principal target organisms are fungi of the Ascomycota division which can cause staining, odour and deterioration of materials. Tests conducted to ASTM and EN standard test methods (summarised in Document IIIB 6.7) have confirmed the efficacy of Sporgard WB in paint, paper and gypsum board at the minimum intended use concentrations of 0.05

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7 EFSA Scientific Report (2007) 110, 1-85, Conclusion on the peer review of Fludioxonil, Page 7 of 85
FRAC 2014 Mode of Action Poster FRAC Fludioxonil E2: PP fungicides 12 phenylpyrrole
http://www.frac.info/publication/anhang/2014%20FRAC%20Mode%20of%20Action%20Poster.pdf

to 0.5% w/w depending on the specific product type. The available test results are considered acceptable, but just adequate to allow approval of fludioxonil as a fungicidal active substance for use in material preservation in PT 7, 9 and 10 in combination with other active substances. However, efficacy and protection length should be reviewed at product authorisation stage.

8 HUMAN EXPOSURE ASSESSMENT

8.1 IDENTIFICATION OF MAIN PATHS OF HUMAN EXPOSURE TOWARDS ACTIVE SUBSTANCE FROM ITS USE IN BIOCIDAL PRODUCT

The product Sporgard WB contains 2% (w/w) fludioxonil in combination with the active substances azoxystrobin and thiabendazole. The other two a.s. are not subject of this dossier and will be treated as "substances of concern".

Intended uses:
Fludioxonil is used as a fungicide for material preservation that works by inhibiting the growth of many fungi associated with odours, staining and discoloration and generally prevents deterioration caused by mould and mildew. Fludioxonil itself is only handled by industrial users who manufacture the representative biocidal product, Sporgard WB, and incorporate it into preserved end-use products. Fludioxonil is not used directly by professional users or the general public. End-use products preserved using Sporgard WB are sold for use by professional users and the general public (i.e. consumers). The uses are described below:

Product Type 7: Film preservatives

Sporgard WB is intended to be used as a film preservative in end-use products such as water-based paints and coatings and mineral sealants and fillers. These end-use products are intended to be used indoors. Preserved film products may be used by professionals (e.g. decorators and builders) and non professionals (e.g. for Do-It-Yourself (DIY) activities such as wall coating, tiling or grouting). The preserved products may be applied using a sprayer, a paint brush or roller or an application tool such as a trowel.

End-use products containing the Sporgard WB fungicide are intended to be specialised products which are used to treat targeted areas inside buildings such as walls and ceilings; these products would not be expected to be applied extensively to very large areas. Typical products are ready-mixed (ready to use) anti-fungicide water-based paints and coatings and mineral sealants and fillers.

Product type 9: Preservative for fibre, leather, rubber and polymerised materials

9.02 Preservatives for paper

Sporgard WB is intended to be used to treat paper which is used to produce drywall in order to prevent fungal growth. Drywall, also known as plasterboard, wallboard or gypsum board, consists of a panel of gypsum plaster pressed between two thick sheets of paper and is used in the construction of interior walls and ceilings. Drywall products may be used by professional builders and by non-professionals (e.g. consumers) during DIY tasks.

Product type 10: Masonry preservatives

Sporgard WB is used to treat gypsum plaster used in drywalls (e.g. plasterboard, wallboard or gypsum board) in order to prevent fungal growth. The gypsum plaster is pressed between two thick sheets of paper. Drywall is used to make interior walls and ceilings. Drywall products may be used by professional builders and by non-professional users (e.g. consumers) during DIY tasks. Drywall products can be cut to shape using a saw and drilled to wooden structures to secure them in place.

The intended uses and in-use concentrations are summarised in the Table below.

Summary table of intended uses and concentrations of fludioxonil in end-use products

Biocidal product	Field of use envisaged	Concentration of product in end-use material	Concentration of fludioxonil in end-use material
PT7 Film preservative			
Sporgard WB Fludioxonil 2% w/w content	Paints and coatings (aqueous emulsions) Indoor use	0.15-1.6% w/w	max.0.032% min.0.003% in end-use product
	Mineral sealants and fillers (e.g. grout, mortar) Indoor use	0.08-1.6% w/w	max.0.032% min.0.002% in end-use product
PT9.02 – Paper preservative			
Sporgard WB Fludioxonil 2% w/w content	Paper (drywall lining) Indoor use	0.25-0.5% w/w (dry paper)	max. 0.010% min.0.005% in end-use product
PT10 Masonry preservative			
Sporgard WB Fludioxonil 2% w/w content	Drywall gypsum powder Indoor use	0.05-1.6% w/w	max. 0.032% min.0.001% in end-use product

Human exposure:

In line with the recommendations in the Technical Guidance document (TGD) on Risk Assessment and the Technical Notes for Guidance (TNsG) on Human Exposure to Biocidal Products (2002/2008), an exposure assessment for human health has been carried out for fludioxonil in Sporgard WB and its specified uses, based on a tiered approach. In the first instance, for each exposure scenario, a Tier 1 assessment reflecting worst-case exposure assumptions (e.g. task duration, assuming no protective equipments is worn) has been carried out. Tier 2 refinements have then been considered taking into account the wearing of personal protective equipment (PPE) and respiratory protective equipment (RPE), as appropriate.

For industrial and professional workers, the Tier 1 assessment assumes no PPE is worn. The Tier 2a assessment assumes gloves affording 90% protection to the hands and a coverall is worn (penetration = 20%) but no RPE is used. According to the HEEG Opinion on default protection factors for protective clothing and gloves (2010), when coveralls are worn, the protection is 80% where the challenge is "light" (i.e. less than 200 mg in-use product/min) on the whole body, not including the hands (TNsG 2002, Part 2. P.36). Most activities involving the handling of the biocidal product or treated end-use products are unlikely to result in significant contamination to the body. The use of a clothing penetration factor of 20% is therefore considered to be conservative. Where appropriate, Tier 2b provides a further refinement accounting for the wearing of RPE (10-fold protection).

For non-professionals (consumers), the Tier 1 assessments assume no PPE is worn. Consumers may or may not read the product label: there is the expectation – but little guarantee – that they will comply with instructions for the use of products. Also, consumers have no access to professional PPE and may realistically use only household protective equipment (e.g. gardening or kitchen gloves) to protect their hands. Where appropriate, a Tier 2 refinement assumes household gloves, a long-sleeved shirt, trousers and boots are worn. The TNsG (2002, Part 2, p. 34) and the HEEG Opinion on default protection factors for protective clothing and gloves (TM 1 2010) inform that it is reasonable to assume a reduction in dermal exposure of 50% when a long-sleeved shirt and, trousers or skirt with shoes, but no gloves are worn.

The critical effects associated with exposure to fludioxonil are systemic effects: local effects at the site of contact are not predicted. Systemic exposures to the active substance have been determined via the oral, dermal and inhalation routes for the purpose of comparison with the respective critical endpoint values in the risk assessment.

For an adult (workers and consumers), body weight = 60 kg (ECETOC, 2001 and ECB, 2003, HEEG Opinion on default human factor values for use in exposure assessments for biocidal products, TM II 2013) and inhalation rate = 1.25 m3/hour (TNsG, Part 3, p 63, HEEG 2013). For toddlers, a body weight of 10 kg is assumed (HEEG, 2013).

In a worst-case assessment it is assumed there is 100% absorption of the active substance following inhalation exposure to fludioxonil in Sporgard WB.

For risk assessment purposes, a dermal absorption value of 3% has been used for fludioxonil. It should be noted that this is value is conservative when considering dermal absorption from end-use products such as paints, plaster-board and mineral sealants, where the active substance is bound in a matrix within the treated product or article. For a detailed justification please refe to section 3.1.1 and the section “Dermal absorption”.

Summary table: relevant paths of human exposure							
Exposure path	**Primary (direct) exposure**			**Secondary (indirect) exposure (expected only for PT7)**			
	Industrial use	**Professional use**	**Non-professional use**	**Industrial use**	**Professional use/Non-professional use**	**General public**	**Via food**
Inhalation	No	Yes	Yes	No	Yes	No	No
Dermal	Yes	Yes	Yes	Yes	Yes	Yes	No
Oral	No	No	No	No	No	Yes (toddlers)	No

The primary routes of exposure to fludioxonil when using end-use products preserved using Sporgard WB are the dermal and inhalation routes (exposure via the oral route is not envisaged during normal use). The active substance has a very low vapour pressure (< 1 x 10-6 Pa) and can therefore be considered to be non volatile from solution and preserved end-use products and articles. However, use of the products can result in the formation of sprays and/or mists and therefore inhalation exposure is

considered (however not for industrial use in PT7-1, PT9-1 and PT10-1 ; *Loading liquid, automated or semi-automated*) .

Secondary (indirect) exposure to fludioxonil may arise in professional workers and in non-professionals (i.e. consumers) when removing dried coatings (e.g. paints and sealants) which have been preserved using Sporgard WB. These coatings would typically be removed by sanding and exposures to dusts would arise.

Secondary (indirect) exposure may arise when members of the public come into contact with treated products. Potential exposure may arise via the oral or dermal routes. There is no direct release of the product or active substance to the environment and exposure to humans via release to the environment is considered to be negligible.

The potential for exposure to the product is summarised in the table above.

8.2 LIST OF SCENARIOS

All the human exposure scenarios have been calculated using the highest concentration of Sporgard WB in end-use material of 1.6% w/w (corresponding to 0.032% fludioxonil).

Summary table: scenarios for PT7			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
PT7-1	Mix/load	**Primary:** Mixing and loading, i.e., blending of the biocidal product (b.p.) into the paint	Industrial (PT7)
PT7-2	Maintenac e of machines	**Primary:** Maintenance work is done for the different parts of production machines.	Industrial (PT7)
PT7-3	Spray application	**Primary:** Applying preserved water-based paints by spraying	Professional (PT7)
PT7-4	Brush and roller application	**Primary:** Applying preserved water-based paints using a brush or roller	Professional (PT7)
PT7-5	Application of mineral sealants and grout	**Primary:** Applying preserved mineral sealant or grout	Professional (PT7)
PT7-6	Wash out paint brush	**Primary:** Washing out paint brushes after application	Professional (PT7)
PT7-7	Spray equitment cleaning	**Primary:** Cleaning of spray equipment after application	Professional (PT7)
PT7-8	Spray application	**Primary:** Applying preserved water-based paints by spraying	Non-Professional (PT7)
PT7-9	Brush and roller application	**Primary:** Applying preserved water-based paints using a brush or roller	Non-professional (PT7)
PT7-10	Application of mineral sealants and grout	**Primary:** Applying preserved mineral sealant or grout	Non-professional (PT7)
PT7-11	Wash out paint brush	**Primary:** Washing out paint brushes after application	Non-professional (PT7)
PT7-12	Spray equitment cleaning	**Primary:** Cleaning of spray equipment after application	Non-professional (PT7)
PT7-13	Toddler	**Secondary (in direct exposure):** Toddler – touching wet painted surface	General public (PT7)
PT7-14	Toddler	**Secondary (in direct exposure):** Toddler – touching wet painted surface and mouthing	General public (PT7)

PT7-15	Toddler	**Secondary (indirect exposure)** Toddler – touching dried painted surface	General public (PT7)
PT7-16	Toddler	**Secondary (indirect exposure)** Toddler – touching dried painted surface and mouthing	General public (PT7)
PT7-17	Adult	Adult –laundry of contaminated coveralls after paint spraying activities	General public (PT7)
PT7-18	Toddler	**Secondary (in direct exposure):** Toddler – dermal contact with wet preserved materials (e.g. mineral sealants and grouts)	General public (PT7)
PT7-19	Toddler	**Secondary (in direct exposure):** Toddler – dermal contact with wet preserved materials (e.g. mineral sealants and grouts) and mouthing	General public (PT7)
Scenario (screening) Long term inhalation exposure for volatilised active substance	Toddler	**Secondary (indirect exposure):** Toddler – inhalation exposure to volatilized residues	General public (PT7)
PT7-20	Adult	**Secondary (indirect exposure)** Adult (professional worker) – removing dried preserved paint and sealant by sanding	Professional (PT7)
PT7-21	Adult	**Secondary (indirect exposure)** Adult (non-professional) – removing dried preserved paint and sealant by sanding	Non-professional (PT7)

Summary table: scenarios for PT9			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure** **Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
PT9-1	Mix/load	**Primary:** Mixing and loading; handling concentrate for PT 9.02 uses – paper for drywall manufacture	Industrial (PT9)

Summary table: scenarios for PT10			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
PT10-1	Mix/load	**Primary:** Mixing and loading; handling concentrate during gypsum powder/dry wall manufacture	Industrial (PT10)
PT10-2	Cutting /sawing	**Primary:** Professional cutting/sawing or drilling gypsum drywall	Professional (PT10)
PT10-3	Cutting /sawing	**Primary:** Non-professional cutting/sawing or drilling gypsum drywall	Non-professional (PT10)

8.3 INDUSTRIAL EXPOSURE

8.3.1 Scenario [PT7-1, PT7-2, PT9-1 and PT10-1]

This section considers exposures to fludioxonil which may occur in workers during scenarios where the biocidal product, Sporgard WB, is incorporated into end-use products (treated articles) such as paints (PT 7), industrial paper (PT 9) and masonry products (PT 10).

Sporgard WB may be added to end-use products during the formulation and manufacturing stages at industrial sites. The finished end-use products incorporating the Sporgard WB biocide are then transported to professional users and retails stores.

PT7-1, PT9-1 and PT10-1 Mixing and loading phase – Handling concentrate

Description of Scenario [PT7-1, PT9-1 and PT10-1]: *Mixing and loading handling concentrate into paint* *Industrial worker*		
Mixing and loading phase *Industrial worker handling concentrate for PT7, PT9 and PT10 uses –paint, paper for drywall manufacture and gypsum powder/dry wall manufacture* ***RISKODERM – Loading liquid, automated or semi-automated (HEEG, 2008). Task duration 10 min.*** *Sporgard WB containing 2% w/w fludioxonil.* *Oral exposure is not considered relevant for industrial workers*		
	Parameters[1]	**Value**

Tier I	Potential hands exposure	101 mg/min (95th percentile)
	Potential dermal body exposure	2.02 mg/min (95th percentile)
	Indicative inhalation exposure	Not relevant
	Concentration of active ingredient	2%
	Duration of task	10 min/day
	Body weight (kg)	60
	Clothing penetration	100%
	Dermal absorption	3%
Tier II	Gloves	10% penetration)
	Coverall	(20% penetration)
	no RPE	-

Calculations for Scenario [PT7-1, PT9-1 and PT10-1]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-1]

This scenario addresses the intended use of Sporgard WB in the production of end-use products (e.g. paints) during industrial manufacturing and formulation processes. The intended use of Sporgard WB as a preservative in the manufacture of paints is restricted to workers in an industrial situation. Limited exposures are likely to arise, primarily during mixing and loading activities.
Sporgard WB is incorporated in to end-use products such as paints to prevent fungal growth. The incorporation of the biocidal product into these end-use products takes place using closed and fully automated industrial manufacturing and formulation processes. The potential for exposures to arise is very limited e.g. for less than a minute when connecting or disconnecting pipes or hoses using automated or semi-automated processes.

Sporgard WG is incorporated as a preservative in paints at concentrations up to 1.6% w/w, giving a maximum fludioxonil concentration of 0.032% w/w (based on a concentration of 2% w/w fludioxonil in the product).

The following task has been identified for workers in industrial settings using Sporgard WB during the production of end-use products (e.g. preserved paints), PT7:

Mixing and loading:

Adding concentrated preservative to paint during manufacturing and formulation processes.

This scenario is described in more detail below.

The potential for exposures to fludioxonil to arise in workers during automated industrial manufacturing and formulation processes where Sporgard WB is incorporated into paints is very limited. Activities involving any contact with the process equipment are expected to be less than a minute, for example when connecting or disconnecting pipes or hoses using automated or semi-automated methods. There are no models available which provide a realistic assessment of exposure for these activities. Exposures have therefore been assessed using worst-case reference models and data from the TNsG and HEEG

opinions. These approaches are conservative and the predicted exposures are expected to over-estimate exposures in reality.

To determine exposures in industrial workers during the mixing and loading phase, it is assumed that the workers load Sporgard WB into the paint manufacturing/formulation equipment by connecting and disconnecting the concentrated product to the dosage pump via transfer lines. Dermal exposures to fludioxonil in industrial workers were assessed using the indicative data provided in the HEEG *Opinion on the use of available data and models for the assessment of the exposure of operators during the loading of products into vessels or systems in industrial scale* (April 6, 2008) for liquid (semi-) automated transfer/pumping processes. In the assessment, the 95th percentile indicative exposure values for the hands (**101 mg/min**) and the body (**2.02 mg/min**) from the RISKOFDERM dermal model (*Loading liquid, automated or semi-automated*) were used. Inhalation exposure is not relevant to this scenario.

The contact duration was assumed to be **10 minutes** per day, based on the default value from the TNsG Human Exposure (Excel database of defaults, 2007) and the BEAT worked example for loading of biocide into a closed system (PT 11). This duration has been defined for the decanting of a liquid from one container into another. The actual daily contact time is likely to be much shorter (e.g. the task involves two short twists of the fittings in order to attach or detach a transfer line). The actual daily contact time is not expected to exceed 1 minute. The assessment based on contact duration of 10 minutes is therefore very conservative.

In the Tier 1 assessment it is assumed that no PPE is used. In the Tier 2 assessment, it is assumed that the worker wears gloves (10% penetration) and coveralls (20% penetration).

The dermal absorption of fludioxonil is 3%. The concentration of fludioxonil in Sporgard WB used in the preservation of paints is 2% w/w. The bodyweight of the operator is 60 kg.

Further information and considerations on scenario [PT9-1]

PT 9.02 – Preservatives for paper

This scenario addresses the intended use of Sporgard WB in the production of end-use products (e.g. paper for coating drywall) during industrial manufacturing processes. The intended use of Sporgard WB as a preservative in the manufacture of drywall coating paper is restricted to workers in an industrial situation. Limited exposures are likely to arise, primarily during mixing and loading activities.

Sporgard WB is used to treat paper which is used to produce drywall to prevent fungal growth. Drywall, also known as plasterboard, wallboard or gypsum board consists of a panel of gypsum plaster pressed between two thick sheets of paper and is used in the construction of interior walls and ceilings. The incorporation of the biocidal product into drywall paper takes place using closed and fully automated industrial manufacturing processes. The potential for exposures to arise is very limited e.g. for less than a minute when connecting or disconnecting pipes or hoses using automated or semi-automated processes.

Drywall products may be used by professional builders and by non-professionals (e.g. consumers) during DIY construction tasks. Drywall boards can be cut to shape using a saw and drilled to wooden structures to secure them in place. These processes are unlikely to give rise to significant exposures from the preservatives used to treat the outer paper, but may give rise to dusts of the treated gypsum materials in the core of the drywall. These scenarios are covered under professional and non-professional exposure for preserved masonry (PT10).

Sporgard WG is incorporated as a preservative in paper at concentrations up to 0.5% w/w, giving maximum concentrations of fludioxonil of 0.01% w/w (based on a fludioxonil concentration of 2% w/w).

The following task has been identified for workers in industrial settings using Sporgard WB during the production of end-use products (e.g. preserved paper products), PT9.02

Mixing and loading:

Adding concentrated preservative to industrial paper during manufacture of drywall.

This scenario is described in more detail below.

The potential for exposures to fludioxonil to arise in workers during automated industrial manufacturing processes where Sporgard WB is incorporated into drywall paper is very limited. Activities involving any contact with the process equipment are expected to be less than a minute, for example when connecting or disconnecting pipes or hoses using automated or semi-automated methods. There are no models available which provide a realistic assessment of exposure for these activities. Exposures have therefore been assessed using worst-case reference models and data from the TNsG and HEEG opinions. These approaches are conservative and the predicted exposures are expected to over-estimate exposures in reality.

To determine exposures in industrial workers during the mixing and loading phase, it is assumed that the workers load Sporgard WB into the drywall manufacturing equipment by connecting and disconnecting the concentrated product to the dosage pump via transfer lines. Dermal exposures to fludioxonil in industrial workers were assessed using the indicative data provided in the HEEG *Opinion on the use of available data and models for the assessment of the exposure of operators during the loading of products into vessels or systems in industrial scale* (April 6, 2008) for liquid (semi-) automated transfer/pumping processes. In the assessment, the 95th percentile indicative exposure values for the hands (**101 mg/min**) and the body (**2.02 mg/min**) from the RISKOFDERM dermal model (loading liquid, automated or semi-automated) were used. Inhalation exposure is not relevant to this scenario.

The contact duration was assumed to be **10 minutes** per day, based on the default value from the TNsG Human Exposure (Excel database of defaults, 2007) and the BEAT worked example for loading of biocide into a closed system (PT 11). This duration has been defined for the decanting of a liquid from one container into another. The actual daily contact time is likely to be much shorter (e.g. the task involves two short twists of the fittings in order to attach or detach a transfer line. The actual daily contact time is believed not to exceed 1 minute. The assessment based on contact duration of 10 minutes is therefore very conservative.

In the Tier 1 assessment it is assumed that no PPE is used. In the Tier 2 assessment, it is assumed that the worker wears gloves (10% penetration) and coveralls (20% penetration). The dermal absorption of fludioxonil is 3%. The concentration of fludioxonil in Sporgard WB used in the preservation of paper is 2% w/w. The bodyweight of the operator is 60 kg.

Further information and considerations on scenario [PT10-1]

This scenario addresses the intended use of Sporgard WB in the production of end-use products (e.g. gypsum plaster used in drywalls) during industrial manufacturing processes. The intended use of Sporgard WB as a preservative in the manufacture of gypsum plaster is restricted to workers in an industrial situation. Limited exposures are likely to arise, primarily during mixing and loading activities.

Sporgard WB may be incorporated into end-use products such as gypsum plaster used in drywalls (e.g. plasterboard, wallboard or gypsum board) to prevent fungal growth. The gypsum plaster is pressed between two thick sheets of paper. Drywall is used to make interior walls and ceilings. The incorporation of the biocidal product into these end-use products takes place using closed and fully automated industrial manufacturing and formulation processes. The potential for exposures to arise is very limited e.g. for less than a minute when connecting or disconnecting pipes or hoses using automated or semi-automated processes.

Drywall products are used by professional builders or non-professionals (i.e. consumers) during construction tasks who may cut, saw or drill them using power tools (these scenarios have been addressed in Sections IIB 3.2.3.3 and 3.2.4.3).

Sporgard WB may be incorporated as a preservative in gypsum powder at concentrations up to 1.6%, giving maximum concentrations of fludioxonil of 0.032% (based on a fludioxonil concentration of 2% w/w).

The following tasks have been identified for workers using Sporgard WB in the manufacture of preserved masonry products in industrial settings, PT10.

Mixing and loading:

Adding concentrated preservatives in gypsum during the manufacture of drywall products.

This scenario is described in more detail below.

The potential for exposures to fludioxonil to arise in workers during automated industrial manufacturing processes where Sporgard WB is incorporated into gypsum powder is very limited. Activities involving any contact with the process equipment are expected to be less than a minute, for example when connecting or disconnecting pipes or hoses using automated or semi-automated methods. There are no models available which provide a realistic assessment of exposure for these activities. Exposures have therefore been assessed using worst-case reference models and data from the TNsG and HEEG opinions. These approaches are conservative and the predicted exposures are expected to over-estimate exposures in reality.

To determine exposures in industrial workers during the mixing and loading phase, it is assumed that the workers load Sporgard WB into the gypsum manufacturing/formulation equipment by connecting and disconnecting the concentrated product to the dosage pump via transfer lines. Dermal exposures to fludioxonil in industrial workers were assessed using the indicative data provided in the HEEG *Opinion on the use of available data and models for the assessment of the exposure of operators during the loading of products into vessels or systems in industrial scale* (April 6, 2008) for liquid (semi-) automated transfer/pumping processes. In the assessment, the 95th percentile indicative exposure values for the hands (**101 mg/min**) and the body (**2.02 mg/min)** from the RISKOFDERM dermal model (loading liquid, automated or semi-automated) were used. Inhalation exposure is not relevant to this scenario.

The contact duration was assumed to be **10 minutes** per day, based on the default value from the TNsG Human Exposure (Excel database of defaults, 2007) and the BEAT worked example for loading of biocide into a closed system (PT 11). This duration has been defined for the decanting of a liquid from one container into another. The actual daily contact time is likely to be much shorter (e.g. the task involves two short twists of the fittings in order to attach or detach a transfer line. The actual daily contact time is believed not to exceed 1 minute. The assessment based on contact duration of 10 minutes is therefore very conservative.

In the Tier 1 assessment it is assumed that no PPE is used. In the Tier 2 assessment, it is assumed that the worker wears gloves (10% penetration) and coveralls (20% penetration).

The dermal absorption of fludioxonil is 3%. The concentration of fludioxonil in Sporgard WB used in the preservation of gypsum is 2% w/w. The bodyweight of the operator is 60 kg.

PT7-2 Maintenance of machines

Description of Scenario [PT7-7] **Maintenance of machines**		
Maintenance of machines *Industrial worker conducting maintenance work done for the different parts of the production machines (used in paint manufacture and formulation)* *ECHA Biocides Guidance 2015: Biocides Human Health Exposure Methodology (dermal algorithm)*		
	Parameters*	**Value**
Tier I	The surface area of hands/lower arms[a]	1948.8 cm^2
	The estimated thickness of product on the skin[b]	0.0234 cm
	Concentration of active ingredient	2%
	Duration of task	240 min
	Frequency	One event per year
	Body weight (kg)	60
	Dermal absorption	3%
Tier II	Gloves	10% penetration
	No coverall	-
	No RPE	-

[a]Source: surface area of hands and lower arms from an adult: Table 1, p. 15 (ECHA Biocides Guidance 2015: Biocides Human Health Exposure Methodology)
[b]USEPA Exposure Factors Handbook (2011), Table 7-24 initial contact no wiping

Calculations for Scenario [PT7-2]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-2]

During the industrial manufacture and formulation of paints, where Sporgard WB is added as a preservative, maintenance work may be carried out for different parts of the production machines. Dermal exposure may arise in workers when performing machine maintenance operations. These tasks are expected to last for 4 hours and would be carried out infrequently, e.g. once per year.

Potential dermal exposure to the concentrate, Sporgard (WG) has been calculated for a thin film of active substance on the worker's hands and forearms using the algorithm: Amount of Sporgard WB on skin = density of concentrate (g/cm3) x layer thickness (cm) x skin contact area (cm2). Systemic exposure to the fludioxonil was determined by accounting for 2% active substance in Sporgard WB, a dermal aborption value of 3% and an operator bodyweight og 60 kg.

In the Tier 1 assessment it is assumed that no PPE is used. In the Tier 2 assessment, it is assumed that the worker wears gloves (10% penetration).

Summary table: systemic exposure from industrial uses				
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake**	**Estimated dermal uptake (mg fludioxonil/kg bw/day)**	**Estimated total uptake (dermal + inhalation) (mg fludioxonil/kg bw/day)**
Scenario [PT7-1]	Tier I Tier II	NA NA	$1.0x10^{-2}$ $1.1x10^{-3}$	$1.0x10^{-2}$ $1.1x10^{-3}$
Scenario [PT7-2]	Tier I Tier II	NA NA	0.46 $4.6x10^{-2}$	0.46 $4.6x10^{-2}$
Scenario [PT9-1]	Tier I Tier II	NA NA	$1.0x10^{-2}$ $1.1x10^{-3}$	$1.0x10^{-2}$ $1.1x10^{-3}$
Scenario [PT10-1]	Tier I Tier II	NA NA	$1.0x10^{-2}$ $1.1x10^{-3}$	$1.0x10^{-2}$ $1.1x10^{-3}$

8.3.2 Combined scenarios

Scenarios combined	**Estimated inhalation uptake**	**Estimated dermal uptake (mg fludioxonil/kg bw/day)**	**Estimated total uptake (mg fludioxonil/ kg bw/day)**
Industrial workers: Mixing and loading/blending biocidal product into the paint (PT7-1) and maintenance activities (PT7-2) – **Tier I**	NA	0.47	0.47
Industrial workers: Mixing and loading/blending biocidal product into the paint (PT7-1) and maintenance activities (PT7-2) – **Tier II**	NA	$4.7x10^{-2}$	$4.7x10^{-2}$

*

Industrial workers may carry out a number of tasks during a working shift where exposures to fludioxonil may arise. Combined exposures have been considered for the following scenarios:

- Industrial workers – conducting mixing and loading tasks (PT7-1 mixing and loading : blending of the biocidal product into the paint) - in conjuction with maintenance activities (PT7-2)

8.4 PROFESSIONAL EXPOSURE

This section considers exposures to fludioxonil which may occur in professional workers during the application of end-use products which have been preserved using Sporgard WB such as paints (PT 7) and masonry products (PT 10).

8.4.1 Scenario [PT7-3 to PT7-7 & PT10-2]: Professional primary exposure scenarios

Professional exposure: preserved film products (PT7)

Sporgard WB and similar formulations may be used in paints and mineral sealants and grouts to protect the finished films against fungal growth. Sporgard WB and similar formulations are added to these end-use products to give a maximum concentration up to 1.6% w/w of the product, equivalent to 0.032% w/w fludioxonil (based on a fludioxonil concentration of 2% w/w). The end use products can be applied using a sprayer, a brush or roller or an application tool such as a trowel depending on the particular use of the product.

End-use products containing the Sporgard WB fungicide are intended to be specialised products which are used to treat targeted areas inside buildings such as walls and ceilings (these products would not be expected to be applied extensively to very large areas). Unlike other more general painting products which could be applied daily by professional workers, it is expected that these fungicide-based products may be applied on 1-2 days per week or, less frequently (e.g. 1-2 days per month) however still resulting in many workdays per year and therefore considered to be repeated long-term exposures (which is also in line with other peer reviewed active substance in PT7 products).

Water-based paints containing Sporgard WB may be applied by professional painters in the construction or refurbishment industry (e.g. at site work, or in domestic and office premises). These products are used indoors and applied to walls or ceilings by brush and roller applications or by spraying for example using an electrically powered hand-held medium pressure sprayer such as an air sprayer or a high-volume, low pressure (HVLP) sprayer. Adequate ventilation is recommended during paint application.

During brushing, ready to use paints are typically applied directly from the can without further dilution. For applications using a roller, painting products can sometimes be poured undiluted into another containing (e.g. a roller tray or tub which enables the paint to be readily and uniformly applied to the roller). For spraying operations, ready to use paint may be loaded, or poured into the spraying equipment. The TNsG (2008) Excel Database on Human Exposure informs that ready-for-use paints containing film preservatives do not require mixing calculations because potential exposure arising during the mixing and loading phase are already accounted for in the default data for the application phase. After application, paints form a film and dry. The potential for exposure is greatly reduced and post-application exposure is insignificant. During equipment clean-up, workers may come into contact

with the product which is further diluted by water. Exposure has been assessed for operations involving the application of water-based paints using a sprayer, a brush or a roller.

Mineral sealants and fillers (e.g. grout, mortar etc) are construction materials used to connect sections of pre-cast concrete, fill voids and seal joints (e.g. between tiles). Mineral sealants are generally a mixture of water, cement and sand and may have a colour tint. Dried mineral sealants used in wet rooms (e.g. bath or shower) are prone to colonisation by fungi and Sporgard WB may be added to these products to prevent fungal growth. Since Sporgard WB is a liquid, mineral sealants and fillers into which the biocide is incorporated are expected to be ready-mixed end-use products which can be directly applied from their containers as thick pastes which dry over time (i.e. they are not powder type products which require mixing with water prior to use).

The following tasks have been identified for professionals using preserved film products, PT7.

Mixing and loading (Sporgard WB exposure scenario):

Paints – mixing and loading is minimal

Application (Sporgard WB exposure scenario):

Spraying
Brush and roller
Applying mineral sealants and grouts

Post-application phase (Sporgard WB exposure scenario):

Cleaning out paint brushes after painting
Cleaning out spraying equipment after painting

Mixing and loading phase

The TNsG (2008) Excel Database on Human Exposure informs that ready-for-use paints containing film preservatives (PT 7) do not require mixing calculations because potential exposure arising during the mixing and loading phase are already accounted for in the default data for the application phase. Separate calculations for the mixing and loading phase have not therefore been carried out.

PT-7 Spray application:

Description of Scenario [PT7-3] Spray application		
Professional applying preserved water-based paints by spraying[2] BEAT scenario: Spray application of masonry preservatives (remedial biocides) Task duration 360 min		
	Parameters*	**Value**
Tier 1	Actual hands exposure (inside gloves)	13.2 mg/min (75th percentile)*
	Potential dermal body exposure	365.4 mg/min (75th percentile)*
	Indicative inhalation exposure	136.5 mg/m³ (75th percentile)*
	Concentration of active ingredient	0.032%

	Duration of task	360 min/day
	Body weight (kg)	60
	Clothing penetration	100%
	Dermal absorption	3%
Tier IIa**	Coverall	20% penetration
Tier IIb**	Coverall	20% penetration
	RPE	90% protection (APF10)

*values corrected for the density of preserved paints

Calculations for Scenario [PT7-3]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario *[PT7-3]*

Professionals may be exposed to fludioxonil when applying water-based paints containing Sporgard WB using a sprayer, indoors. However, this application includes only small interior projects. For the application of paints and coatings to interior walls, ceilings and other surfaces, conventional powered sprayers are normally used which spray with 4 to 7 bar pressure. Potential exposures may occur via the dermal route, mainly due to the deposition of generated droplets on the work clothing of professional workers, especially during overhead spraying. Dermal exposures may also occur via spills, leaks from the spray nozzle and from touching contaminated equipment. Potential inhalation exposures to aerosolised particulates have also been considered. Due to their specialised nature, professional painters are not expected to work with these products every day (e.g. 1-2 times per week, or less frequently: 1-2 times per month).

The TNsG (2008) Excel Database on Human Exposure informs that the default value for the total duration of spray painting tasks using products containing film preservatives is 6 hours (360 minutes) **per day**. However, workers would be expected to carry out other preparation activities such as cleaning areas prior to treatment and covering surfaces, and applying other paints, as well and 360 minutes might well be an overestimate. However to keep consistency with other PT21 substances evaluated the default value of 360 minutes has been used..

Exposures have been assessed, taking into account HSE survey data related to the application of remedial biocides to structural timbers and masonry in industrial, recreational and residential settings, using a hand-held medium pressure sprayer which gives a medium/coarse spray. According to the User Guidance 2002 (Annex 4) *Indicative exposure values*, these data are also considered to apply to other operations involving spray applications using electrical or fuel-driven pump-pressurised sprayers supplied from a reservoir. These datasets were incorporated into Spraying Model 2 *"Professional mixing and loading liquids in reservoir for powered spray application at 4 to 7 bar pressure as a coarse of medium spray, indoors and outdoors, overhead, and downwards" (TNsG 2002, Part 2, p146))* but were subsequently included in the Bayesian Exposure Assessment Tool (BEAT) and re-evaluated. Exposures to fludioxonil during spray painting have therefore been assessed using the BEAT model "Spray application of masonry preservative". This model incorporates the HSE dataset for remedial biocides (i.e. based on the application of remedial biocides to internal and external structural timber, masonry, surfaces and to wooden articles using an electrical or fuel driven-pump-pressured sprayer supplied from a reservoir; medium pressure spraying at 4-7 bar) and includes mixing, loading and application phases. The remedial biocides dataset in BEAT contains 67 records based on measured data. Statistical analysis within BEAT indicates that the datasets within these records for potential body, actual hand and inhalation exposure are best represented by log-normal distributions respectively.

Taking into account the moderate uncertainty in the data (i.e. considering the confidence intervals around given percentiles), the 75th percentile values of these datasets is suggested as appropriate indicative exposure values:

Potential body exposure:	261 µL/min (BEAT)
Actual hand exposure (inside gloves):	9.4 µL/min (BEAT)
Inhalation exposure:	97.5 µL/m³ (BEAT)

The indicative data in BEAT are expressed as deposition rates of end-use remedial products as liquid volume. To determine the deposition rate of end-use products in mg, it is necessary to consider the density of the end-use products. In the BEAT scenario, the viscosity of the water-based paints is assumed to be like water having a density close to 1 g/ml (e.g. the products are applied as a surface wash). The density of typical painting and coatings treated with Sporgard WB is expected to be denser, approximately 1.4 g/ml. The indicative data from BEAT have therefore been transformed via the density of preserved paints giving:

Potential body exposure:	**365.4 mg/min**
Actual hand exposure (inside gloves):	**13.2 mg/min**
Inhalation exposure:	**136.5 mg/m³**

[Note: According to the TNsG 2008, p9 – While the expression of the deposition rate for liquids is often used interchangeably with µL/min for water based formulations with a density close to 1, for liquids generally, expressing exposures in µL/min and using a w/v concentration for the active substance will avoid the need to making a correction for density. In this case, using a concentration of Sporgard WB of 2.24 % w/v instead of 1.6 % w/w and the BEAT indicative values in µL/min would give equivalent results to those obtained using the transformed data discussed above].

Tier 1 assumes gloves as the only PPE since hand exposure values are inside gloves). Tier 2a assumes professionals wear coveralls, gloves & shoes. The protection from clothing is 80 %. However, 95% could be also considered as the challenge is "considerable" (i.e. at or above 200 mg in-use product/minute) on the whole body but not including the hands (HEEG opinion on default protective factors for protective clothing and gloves; TNsG 2002, Part 2 p. 36, TNsG 2002, Part 3, p. 60 and TNsG 2007, Table 2, p.19). Impermeable coveralls should provide a high degree of protection against heavy contamination by being relatively resistant to the penetration of the biocides through the material of which the coverall is made. In a further assessment (Tier 2b) it is assumed that RPE (e.g. a respirator) is worn giving 90% protection (APF 10).

The dermal absorption of fludioxonil is 3%. The concentration of fludioxonil in Sporgard WB used in the preservation of paints and coatings is 2% w/w, giving a maximum fludioxonil concentration of 0.032% w/w in end use material (**Table IIB 3.1-1**).

The maximum concentration of Sporgard WB in paints and coatings is 1.6% w/w. The bodyweight of the operator is 60 kg.

PT-7 Brush and roller application:

Description of Scenario [PT7-4] Brush and roller application
Professional applying preserved water-based paints using a brush or roller BEAT scenario: Indoors decorative painting (PT7) Task duration 360 min

	Parameters*	**Value**
Tier I	Potential hands exposure	16.5 mg/min (95th percentile)*
	Potential dermal body exposure	120.4mg/min (95th percentile)*
	Indicative inhalation exposure	58.8 mg/m³ (95th percentile)*
	Concentration of active ingredient	0.032%
	Duration of task	360 min/day
	Body weight	60 kg
	Clothing penetration	100%
	Dermal absorption	3%
Tier II	Gloves	10% penetration
	Coverall	20% penetration

*values corrected for the density of preserved paints

Calculations for Scenario [PT7-4]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario *[PT7-4]*

Professionals may be exposed to the active substance when applying Sporgard WB treated surface coatings and pastes indoors using a brush, or for more liquid products, a roller. Potential exposure is via the inhalation and dermal routes. Professional painters may protect their hands with gloves by the nature of their work. Due to the specialised nature of the products treated with Sporgard WB, professional painters are not expected to work with these products every day (e.g. 1-2 times per week, or less frequently: 1-2 times per month).

The TNsG (2008) Excel Database on Human Exposure informs that the default value for the total duration of painting tasks using products containing film preservatives is **6 hours (360 minutes) per day**. This is conservative as workers would be expected to carry out other preparation activities such as cleaning areas prior to treatment and covering surfaces.

There is no specific model for the application of paints on interior walls. Exposure has been assessed using BEAT and a worked example from the BEAT database for film preservatives (PT7): Indoor decorative painting. The scenario describes a professional decorator painting indoor wooden fitments using a small brush and a water based paint. However, in the scenario, indicative data for exposures to the body and via inhalation have been derived from a "garden timber treatment" dataset, comprising 15 data records. The dataset is based on non-professionals brush painting outdoor garden sheds and fences with solvent based wood preservatives direct from the can. Statistical analysis within BEAT indicates that the datasets for exposures to the hands, body and via inhalation indicate that the data are best represented by a log-normal distribution but is considered to apply to indoor scenarios also. Taking into account high uncertainty in the data for potential body exposure and inhalation, the 95th percentile values of the relevant datasets are suggested as appropriate indicative exposure values. Due to the limited number of data points obtained in the study for hand exposures, the indicative value for potential dermal exposure is determined as the 75th percentile value the pooled data from Roff (water) and garden timber treatment. The indicative data given in BEAT for indoor decorating painting are:

Potential body exposure (professional): 86 µL/min (BEAT)
Potential hand exposure: 11.8 µL/min (professional, BEAT)
Inhalation exposure: 42 µL/m³ (professional, BEAT)

The indicative data in BEAT are expressed as deposition rates of end-use products as liquid volume. To determine the deposition rate of end-use products in mg, it is necessary to consider the density of the end-use products. In the BEAT scenario, the viscosity of the solvent-based paints (wood preservative) is assumed to be like water. The density of typical painting and coatings treated with Sporgard is expected to be denser; approximately 1.4 g/ml. As a worst-case approach, the indicative data from BEAT and TNsG 2008 have been transformed via the density of the preserved paint giving:

Potential body exposure (professional): **120.4 mg/min**
Potential hand exposure: **16.5 mg/min**
Inhalation exposure: **58.8 mg/m³**

In the Tier 1 assessment it is assumed that no PPE is used. In the Tier 2 assessment, it is assumed that the worker wears gloves (10% penetration) and coveralls (20% penetration).

The dermal absorption of fludioxonil is 3%. The concentration of fludioxonil in Sporgard WB used in the preservation of paints and coatings is 2% w/w.

The maximum concentration of Sporgard WB in paints and coatings is 1.6% w/w giving a maximum fludioxonil concentration of 0.032% w/w.

PT-7 Application of mineral sealants and grout:

Description of Scenario [PT7-5] Application of mineral sealants and grout		
Professional applying preserved mineral sealant or grout ConsExpo model v.4.1 and default scenario for joint sealant (RIVM DIY Products Factheet p. 59) Inhalation exposure: ConsExpo model: "Exposure to vapour" (Release mode: Evaporation; evaporation from increasing area) Dermal exposure: ConsExpo model: "Constant rate" Task duration: 60 minutes; worker remains in room for 480 mins		
	Parameters*	**Value**
Tier 1	Vapour pressure fludioxonil	3.9 x 10^{-7} Pa
	Molecular weight fludioxonil	248.2 g/mol
	Concentration of active ingredient	0.032%
	Inhalation exposure	
	Exposure duration	480 minutes
	Application duration	60 minutes
	Product amount	150 g
	Room volume	10 m^3
	Ventilation rate	2 h^{-1}
	Release area	500 cm^2
	Temperature	20°C
	Mass transfer rate	Langmuir
	Molecular weight matrix	3000 g/mol

	Inhalation rate	1.25 m^3/hr
	Adult Body weight	60 kg
	Dermal exposure	
	Contact rate	50 mg/min
	Release duration	60 minutes
	Dermal absorption	3%
Tier II	Gloves	10% penetration

Calculations for Scenario [PT7-5]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario *[PT7-5]*

Professional workers may be exposed to fludioxonil when applying mineral sealants and fillers (e.g. tiling grouts preserved using Sporgard WB). These end-use products are typically supplied in ready-mixed formulations in tubs or other containers. Using a trowel or scraper, they may be applied to surfaces directly from their containers as thick pastes which dry over time (i.e. they are not powder type products which require mixing with water prior to use). No mixing and loading or post-application clean-up is required. Potential exposure may occur via the dermal route (i.e. as contamination of hands during the application of product) but is expected to be minor as the products would usually be handled using an application tool. Furthermore, hands will be washed after application. Inhalation exposures are unlikely, but have nevertheless been considered in a worst case approach. Due their specialised nature, professional workers are unlikely to use these products every day (e.g. 1-2 times per week or less frequently: 1-2 times per month)

There are no models or data provided in the TNsG on potential exposures arising from the use of mineral sealants or grouts by professional workers. While several models are available in ConsExpo 4.1 and the associated RIVM Factsheet for DIY products[8] for the scenarios involving the application of sealants and fillers, there are no specific default datasets which apply to use of ready-for-use mineral-type sealants or grouts. by professional workers. However, since the ConsExpo model and the corresponding RIVM DIY Product Factsheets contain detailed information for the use of sealants, it is considered that an modification of the approach for the consumer can be applied to the assessment of exposures in professional workers.

[8] RIVM report 320104007/2007; Do-It-Yourself Products Fact Sheet - To assess the risks for the consumer, W. ter Burg, H.J. Bremmer, J.G.M van Engelen, page 57

Dermal and inhalation exposures are predicted using the ConsExpo 4.1 model and the corresponding parameters for the default scenario: Joint sealant provided in the RIVM DIY Products Factsheet Section 4.1.1., p. 59, adapted for professional users. The scenario for joint sealants is assumed to be performed in a bathroom (moist environment). This describes a scenario where the joints between a bathtub, shower cabinet or washstands and wall will be sealed off. The total joint length when sealing off the joints is assumed to be 5 metres. It is expected that professional workers (e.g. tile fitters or plumbers), would apply greater quantities of sealant for longer task durations than consumers. For example, when working in a domestic bathroom setting, a tiler or plumber may be expected to seal off a bathtub as well as other fittings (e.g. toilets, sinks, tiling edges, window sills etc). The default model in ConsExpo, has therefore been adapted accordingly. It is assumed that professional workers will work daily (e.g. 5 days / week; 220 days per year).

Inhalation exposure during the task was assessed using the ConsExpo model "Exposure to vapour", set in the evaporation (evaporation from an increasing area) mode of release. The total joint length between a bathtub and wall is estimated to be 5 metres and requires 75 ml of sealant. Assuming the density of the sealant is 1 g/cm^3, the amount of product used will be 75g. In addition, the worker uses a further 75 ml to seal off other fittings in the bathroom , such that the total amount of product used in 150 g. While the default application duration is set at 30 minutes for a consumer, since the worker is assumed to apply twice as much sealant, the application duration is considered to be 60 minutes. As a worst-case scenario, the worker is assumed to spend a full working shift in the room where the sealant has been used, to account for other tasks which will be performed. The exposure duration is therefore 480 minutes. The default values for the volume of the bathroom and the ventilation rate respectively are: 10 m^3 and 2 hr^{-1}. The release area is 500 cm^2; determined as two strips of sealant 5 m long and 5 mm wide, respectively. The Langmuir method has been used to determine the mass transfer rate since this is the default approach. The molecular weight matrix has been set at 3000 g/mol: the default for DIY products (considered to apply also to products used by professional workers). Inhalation exposure was determined as the internal dose on the day of exposure (e.g. the absorbed dose per kg bodyweight during one day).

Dermal exposure was determined using the ConsExpo "Constant rate" direct contact model where the dose is expressed as a function of the rate at which the product is applied to the skin, the loading time, the weight fraction of fludioxonil and the bodyweight. It is assumed that exposure will be to the fingertips only when used to smoothen down the applied sealant (skin surface area = 2 cm^2). The contact rate has been assumed to be 50 mg/min (the dermal load is expected to be significant), Dermal exposure was determined as the internal dose on the day of exposure (e.g. the absorbed dose per kg bodyweight during one day)

The dermal absorption of fludioxonil is 3%. The concentration of fludioxonil in Sporgard WB used in the preservation of mineral sealants and fillers is 2% w/w. The maximum concentration of Sporgard WB in mineral sealants and fillers is 1.6% w/w (giving a maximum fludioxonil concentration of 0.032% w/w in end use material.

In a Tier 1 assessment, it is assumed that no gloves are worn whereas in a Tier 2 assessment, it is assumed that gloves affording 90% protection of the hands are worn.

PT-7 Post-application phase - Cleaning out paint brushes:

Description of Scenario [PT7-6] **Wash out paint brush**		
Professional washing out paint brushes after application HEEG opinion 2008		
	Parameters	**Value**
Tier 1	Brush size: 10 x 10 x 2 cm (large brush, worst case)	200 ml
	Volume of paint remaining in brush after painting	1/8 of brush size = 25 ml
	Density of water-based paint	1.4 g/mL
	Volume of each washing solution:	at least 400 ml
	Percentage of residues remaining in brush after each washing step:	10%
	Following each washing step, percentage of residues squeezed out of brush:	50%
	Percentage of residues squeezed out of brush which are absorbed by the cloth:	90%
	Concentration of active ingredient	0.032%
	Body weight	60 kg
	Dermal absorption	3%
Tier II	Gloves	10% penetration

Calculations for Scenario [PT7-6]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario *[PT7-6]*

After applying paint products preserved with Sporgard WB, professionals may potentially be exposed to fludioxonil when cleaning out equipment after use, e.g. washing out brushes. Exposures were assessed using the approaches set out in the HEEG Opinion on Washing out Brushes. To attempt to estimate the potential exposure to the skin of hands during this activity, a worst-case scenario has been assessed. This scenario will usually be used for application of non-water-based paints because for water-based paints, the brush will often be cleaned under a running tap, the running water washing both the paint from the brush and any paint contamination from the hands. In this case, this scenario is not relevant to Sporgard WB products which are water based, but may be applicable to other non-water based paints which contain the active substance.

Cleaning the brush used for applying paint may be done by repeated dipping and swilling in a vessel containing solvent. A large brush might have a size of 10 x 10 x 2 cm, corresponding to a volume of 200 ml. It is assumed that after painting one eighth (1/8) of the brush volume is paint. Cleaning is assumed to be done in three steps, each time using fresh solvent. The volume at each step should be large enough to allow sufficient dilution of the residues in the brush. For a brush having a volume of 200 ml the volume of cleaning solvent would be at least 400 ml per step. Each washing step is assumed to result in a *ca* 10-fold dilution of the residues in the brush (i.e. 10% of the paint originally on the brush remains after one washing). After each step the brush is assumed to be squeezed by hand. It is assumed that with this step 50% of the solution in the washed brush is released and may contaminate the hand. However, it

is further assumed that the squeezing is not done by the bare hand but rather by wrapping it first with a cloth, which absorbs 90% of the released liquid. Washing and squeezing may be done 3 times each at maximum.

The relevant default parameters used in the calculation are summarised as follows:

Brush size: 10 x 10 x 2 cm (large brush, worst case) 200 mL
Volume of paint remaining in brush after painting 1/8 of brush size = 25 mL

Density of water-based paint is assumed to be 1.4 g/mL
Volume of each washing solution: at least 400 mL
Percentage of residues remaining in brush after each washing step: 10%
Following each washing step, percentage of residues squeezed out of brush: 50%
Percentage of residues squeezed out of brush which are absorbed by the cloth: 90%

The scenario for washing out a brush reflects a worst-case situation which assumes all contamination on hands at the end of the activity remains there and is available for absorption through the skin.

Tier 1 assumes no PPE is used. Tier 2 assumes gloves (10% penetration) are worn.

PT-7 Post-application phase - Cleaning of spray equipment

Description of Scenario [PT7-7] **Spray equipment cleaning**		
Professional cleaning out spray equipment after application BEAT indicative data Task duration 30 min		
	Parameters*	**Value**
Tier I	Potential hands exposure	50.1 mg/min (75th percentile)*
	Potential dermal body exposure	26.9 mg/min (75th percentile)*
	Indicative inhalation exposure	Neglible
	Concentration of active ingredient	0.032%
	Duration of task	30 min/day
	Body weight	60 kg
	Dermal absorption	3%
Tier II	Gloves	10% penetration
	Coverall	20% penetration

**values corrected for the density of preserved paints

Calculations for Scenario [PT7-7]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario *[PT7-7]*
After applying preserved products by spraying, professionals may potentially be exposed to fludioxonil when cleaning out equipment after use, e.g. cleaning out spray equipment.

Exposure during cleaning of spray equipment is calculated using model from BEAT (Ad Hoc working group on Human Exposure, Recommendation 4, agreed at WG IV 2014). Exposures were assessed using indicative values from the BEAT database (Delgado P., Porcel, J., Abril I., Torres., Teran A, Zugasti A (2004) Potential dermal exposure during the painting process in car body repair shops. *Annals of Occupational Hygiene (48) 229-236*). The data are based on measurements taken in SMEs of the cleaning of a spray gun, carried out in many different ways. The spray guns were usually cleaned with water and later the parts that still remain dirty are rubbed with paper, a rag or a brush, using water or any cleaning solution. The mean sampling time was 3.7 minutes. The scenario comprised several different activities. The main body regions exposed during the cleaning of the spray gun are the hands, though there might be splashes to other parts of the body. The dataset for cleaning of spray equipment in the BEAT database comprises 30 records. It is assumed that workers will spend **30 minutes** cleaning out spray equipment.

The following indicative data were used:

Potential hand exposure: the 90% confidence interval for the 75th percentile is given as 21 to 59, suggesting that the 75th percentile is the appropriate indicative exposure value: 35.8 µL/min = 0.0358 mL/min.

Potential body exposure: the 90% confidence interval for the 75th percentile is given as 14 to 25, suggesting that the 75th percentile is the appropriate indicative exposure value: 19.2 µL/min = 0.0192 mL/min.

Exposure via inhalation associated with cleaning spray equipment is expected to be negligible.

The density of water-based paint is assumed to be 1.4 g/mL. Taking the density of paint into account, the indicative values for hands and the body are 0.05012 g/min (**50.1 mg/min**) and 0.02688 g/min (**26.9 mg/min**), respectively.

In the Tier 1 assessment it is assumed that no PPE is used. In the Tier 2 assessment, it is assumed that the worker wears gloves (10% penetration) and coveralls (20% penetration).

The dermal absorption of fludioxonil is 3%. The concentration of fludioxonil in Sporgard WB used in the preservation of paints is 2% w/w giving a maximum fludioxonil concentration of 0.032% w/w in end use material.

PT-9 Professional exposure: preserved materials (PT9)

There are no direct professional uses of drywall coating paper which has been treated with Sporgard WB as a preservative. The treated drywall coating paper is used to manufacture drywall (e.g. plasterboard) end-use products which may be used by professional workers during construction tasks. Potential exposures arising from the use of drywall products are described further in the section below for professional exposure for preserved masonry PT-10.

PT-10 Application phase: - cutting/sawing or drilling gypsum drywall[1]

Description of Scenario [PT10-2] Cutting/sawing or drilling gypsum drywall		
Professional cutting/sawing or drilling gypsum drywall[1] ECETOC TRA V3 model – workers 240 minutes per day		
	Parameters[1]	**Value**
Tier 1	Concentration of active ingredient	0.032%
	Duration of task	240 minutes per day (4 hours)
	Default value dermal exposure	2.83 mg/kg bw/day[9]
	Default value inhalation exposure	1.8 mg/m^3
	External day dose for a 70 kg person	198 mg/day[10]
	Dermal absorption	3%

[1]Oral exposure is not considered relevant for professionals

Calculations for Scenario (PT10-2)

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT10-2]

Sporgard WB is used to treat gypsum plaster used in drywalls (e.g. plasterboard, wallboard or gypsum board) to prevent fungal growth. The gypsum plaster is pressed between two thick sheets of paper. Drywall is used to make interior walls and ceilings. Drywall products may be used by professional builders during construction tasks who may cut, saw or drill them using power tools. Mixing and loading, and post-application phases are not relevant. Exposure may arise during the application of the products (e.g. cutting to size or fixing to structures using a drill). Sporgard WB is incorporated as a preservative in gypsum powder at concentrations up to 1.6%, giving maximum concentrations of

9 The ECETOC Technical Guide No 114 (Appendix C) provides the default values for corresponding process categories (PROC) for professional use scenarios. PROC 24 was considered applicable to scenario PT10-2. The default dermal exposure value for the task described by PROC 24 is 2.83 mg/kg bw/day. No modifier were applied to this value (e.g. to account for task duration) since the product would be a dusty solid and may be retained on the skin beyond the cessation of the task. This value has been scaled by the bodyweight used in the ECETOC model (e.g. 70 kg) to derive a value for the total amount of product (e.g. gypsum/drywall dust) deposited on the hands: 198.1 mg product/day. This value has then been adjusted accordingly by the default workers bodyweight of 60 kg, the conc of Sporgard and fludioxonil and the dermal absorption value to obtain the systemic exposure value.

10 The ECETOC Technical Guide No. 114 (Appendix A) provides the default values for PROC 24. The product is considered to have low fugacity therefore the "starting" default value for a professional worker has been taken as 3 mg/m^3. To this, a modifier of x 0.6 has been applied to account for the task duration (1-4 hrs) to give an air concentration for the task of 1.8 mg/m^3 which has been taken forward as the "indicative" value for this task.

After the Peer Review process Germany had the following comment to the default values choosen which might need further considerations "In PROC 24 a default value for a professional worker has been taken as 3 mg/m^3. To this, a modifier of x 0.6 has been applied to account for the task duration (1-4 hours) to give an air concentration of 1.8 mg/m3. In our opinion this value is valid for 8 hours. A further refinement with the duration of exposure (240 min) for the systemic exposure leads to an underestimation".

fludioxonil of 0.032% (based on a fludioxonil concentration of 2% w/w). The following tasks have been identified for professionals using preserved masonry products, PT10.

Application:
Cutting, sawing or drilling drywall during construction tasks using power tools.

This scenario is described in more detail below

Application phase

Professional workers may be exposed to fludioxonil when working with drywall products preserved using the Sporgard WG biocidal product. For example, builders would be required to cut, saw or drill the drywall during construction tasks using power tools. These processes may generate dusts of gypsum material held together by the paper coating which may be inhaled. Workers may also be exposed via dermal contact with the dust. There are no data available on the duration of time workers spend carrying out such tasks. As a worst case scenario it is assumed workers spent between 1 and 4 hours per day working with drywall products (**240 minutes** was used in the calculation).

There are no models or data available in the TNsG to assess potential exposures arising from the cutting, sawing or drilling of drywall products. As a worst case scenario exposures have been assessed using default data in the ECETOC Targeted Risk Assessment (TRA) model version 3 - Workers. This model provides a screening level assessment of exposures associated with typical industrial and professional tasks for the purposes of assessing the potential health risks of chemicals. Default data are provided for the scenario: high mechanical energy work-up of substances bound in materials and/or articles (e.g. grinding, mechanical cutting, drilling or sanding; Process code (PROC 24).

Exposure is predominately expected to be to dust. Dermal exposures are to hands. Default values for these tasks carried out indoors (without the uses of any local exhaust ventilation), for 1 to 4 hours per day are **2.83 mg/kg bw/day** and **1.8 mg/m^3** for dermal and inhalation exposures respectively (Appendix C: ECETOC TRA Version 3: Background and Rationale for the Improvements, Technical report No 114). The external day dose of gypsum powder is assumed to be **198 mg/day** (the ECETOC TRA assumes an adult has a bodyweight of 70 kg; the external dose used in the calculation = 70 kg x 2.83 mg/kg bw/day and therefore represents worst case with respect to external dose in this case).

Summary table: systemic exposure from professional uses				
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake** **(mg fludioxonil/kg bw/day)**	**Estimated dermal uptake** **(mg fludioxonil/kg bw/day)**	**Estimated total uptake** **(mg fludioxonil/kg bw/day)**
Application phase				

Scenario [PT7-3] **Spray application**	**Tier I** (gloves; no other PPE)	5.5×10^{-3}	2.2×10^{-2}	2.7×10^{-2}
	Tier IIa (gloves, coveralls, penetration = 20%; no RPE)	5.5×10^{-3}	5.0×10^{-3}	1.0×10^{-2}
	Tier IIb (gloves, coveralls, penetration = 20%; RPE: 10-fold protection)	5.5×10^{-4}	5.0×10^{-3}	5.5×10^{-3}
Scenario [PT7-4] **Brush and roller application**	**Tier I** (no PPE)	2.3×10^{-3}	7.9×10^{-3}	1.0×10^{-2}
	Tier II (PPE: gloves, penetration = 10%, coverall, penetration = 20%)	2.3×10^{-3}	1.5×10^{-3}	3.8×10^{-3}
Scenario [PT7-5] **Applying preserved mineral sealant or grout***	Tier 1 (no gloves)	3.0×10^{-8}	$4.8 \times 10^{-4*}$	4.8×10^{-4}
	Tier 2 (gloves, 90% protection)	3.0×10^{-8}	$4.8 \times 10^{-5*}$	4.8×10^{-5}
Scenario [PT10-2] **Cutting/sawing or drilling gypsum drywall**	Tier 1 (no gloves)	4.8×10^{-5}	3.2×10^{-5}	8.0×10^{-5}
	Tier 2 (gloves, 90% protection)	4.8×10^{-5}	3.2×10^{-6}	5.1×10^{-5}
Post-application phase				

Scenario [PT7-6] **Wash out paint brush**	Tier 1 (no gloves)	NA	2.8×10^{-5}	2.8×10^{-5}
	Tier 2 (gloves, penetration = 10%	NA	2.8×10^{-6}	2.8×10^{-6}
Scenario [PT7-7] **Spray equipment cleaning**	Tier 1 (no PPE)	NA	3.7×10^{-4}	3.7×10^{-4}
	Tier 2 (PPE: gloves, penetration = 10%, coverall, penetration = 20%)	NA	5.0×10^{-5}	5.0×10^{-5}

8.4.1 Scenario [PT7-20]: Professional secondary exposure scenarios

Description of Scenario [PT7-20] Adult (professional worker) – Removing preserved paint or sealant by sanding		
Secondary (indirect): Professional worker removes preserved paint or sealant by sanding. Task duration- 6 hrs per day (chronic exposure scenario).		
	Parameters	**Value**
Tier 1	Concentration of active substance	0.032% w/w
	Density of paint	1.4 g/ml
	Concentration of active in dried paint	0.058% w/w
	Inhalation exposure	
	Active substance concentration in 0.1 cm paint layer	0.815 mg/cm^3
	Inhalation rate (intensive activity)	3 m^3/h
	Task duration	6 hrs
	Exposure to wood dust during sanding for 60 minutes	100 mg/m^3
	Density of soft wood	0.4 g/cm^3
	Adult bodyweight	60 kg
	Dermal exposure	
	Highest active substance concentration on painted surface	0.0136 mg/cm^2
	Surface area of both hands	820 cm^2
	Fraction of hands contaminated during prolonged contact	20%
	Transfer efficiency for painted wood	3%
	Dermal absorption	3%

	Adult bodyweight	60 kg

Calculations for Scenario (PT7-20)

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-20]

Professional workers may be indirectly exposed to fludioxonil when removing paint from surfaces which have been painted using a product preserved using Sporgard WB or when removing a preserved sealant by sanding. Inhalation and dermal exposures to dust generated during the sanding process is expected to occur. Exposures during the removal of a sealant are not expected to be any higher that those following the removal of paint. In this case, the assessment will also cover the removal of the sealant by sanding and separate calculations have not been presented. It is assumed that professional workers may be performing sanding operations on a daily basis, for up to 6 hours per day, during a working week, such that this can be considered as a chronic exposure scenario. As a worst-case scenario, it is assumed that sanding is carried out manually. The assessment assumes that no gloves are worn: when handling sanding tools; wearing gloves would not be expected and may potentially be hazardous.

Scenario PT7-21 describes the approach for assessing secondary exposures in a non-professional (i.e. a consumer) when sanding surfaces coated in preserved paint, based on an acute scenario in which one sanding operation of duration 1 hour is performed per day.

Inhalation exposure

In this scenario, it is assumed that a professional worker is sanding a painted surface and the active substance, fludioxonil, is in a paint layer of thickness 0.1 cm. It is assumed that sanding takes 6 hours. Taking into account a concentration of fludioxonil in wet paint of 0.032 % w/w, a paint density of 1.4 g/ml, and a factor of 1.82 to for the higher concentration of active substance in dried paint (Applicant information), the active substance concentration in 0.1 cm paint layer which is sanded is 0.815 mg/cm^2.

As a conservative assumption, according to air measurements made during paint sanding operations in a joinery shop made by the Finnish Institute of Occupational Health (number of measurements: 80, arithmetic mean: 13 mg/m^3, median: 6.3 mg/m^3, range 0.3-81 mg/m^3), during one hour of sanding, the worker would be exposed to wood dust at a concentration of 100 mg/m^3 (Measurement results published in: Liukkonen T, Korhonen K, Lindroos L, Nylund L. Puusepänteollisuuden ke-mikaaliselvitys. Raporttisarja 4. Lappeenrannan aluetyöterveyslaitos, Lappeenranta 1992. 49 s + liitteet. ISBN 951-801-928-2, Liukkonen T, Korhonen K, Lindroos L. Kemikaalit ja niille altistuminen puusepänteollisuudessa. Työ ja ihminen 9:55-66 (1995). It is expected that manual sanding is a more intensive activity that normal working tasks for which a default inhalation rate of 1.25 m^3/hour (light exercise) is assumed. A more representative inhalation rate is therefore assumed to be 3 m^3/hr. The amount of dust inhalation would be: 3 m^3/h x 6 h x 100 mg/m^3 = 1800 mg. Based on a density of soft wood of 0.4 g/cm^3, the volume of dust inhaled would be: (1800 mg/1000)/0.4 g/cm^3 = 4.5 cm^3. The amount of fludioxonil in the wood dust is therefore calculated as: 0.815 mg/cm^3 x 4.5 cm^3 = 3.669 mg/cm^3. The systemic inhalation dose of fludioxonil for a professional worker of bodyweight 60 kg is determined as **6.1 x 10^{-2} mg/kg bw/day.**

As an alternative approach, a reverse reference scenario was used to determine an estimate of the maximum amount of exposure that might be acceptable. The long-term AEL-value of 0.37 mg/kg bw/day was used to calculate the amount of product that would lead to that amount by inhalation. The inhalation rate is assumed to be 3 m^3/h and the task duration is 6 hours. The concentration of fludioxonil in dried paint is 0.058% w/w (i.e. 1.82 times the concentration in wet paint).

The amount of fludioxonil in the paint dust: 0.37 mg/kg /day × 60 kg = 22.2 mg/day
The amount of paint (i.e sanding dust): 22.2 mg/day ÷ 0.058% = 38118 mg/day.

The amount of air inhaled during the task: 3 m^3/h × 6h = 18 m^3

Hence the concentration of sanding dust in the inhaled air is = 38118 mg ÷ 18 m^3 = 2117.7 mg/m^3

According to measurements of the air concentration after paint sanding operations in a joinery shop made by the Finnish Institute of Occupational Health, this is 26 times greater than the maximum measurement result (number of measurements 80, arithmetic mean 13 mg/m^3, median 6.3 mg/m^3, range 0.3-81 mg/m^3).

Dermal exposure (hands – no gloves worn)

The highest concentration of fludioxonil on the preserved surface is determined to be 0.136 mg a.s./cm² (According to the RIVM Painting Products Factsheet, 2.5 L of paint would be applied to walls of a total surface area of 15 m^2, such that the application rate for paint is 0.01667 ml/cm^2. Accounting for a paint density of 1.4 g/ml and that dried paint contains fludioxonil at 0.058 % w/w, the concentration of the active substance in dried paint on the treated surface is 0.0136 mg a.s./cm^2).

The surface area of both hands is 820 cm² and during prolonged and repeated contact, 20% of the hand is contaminated (TNsG 2002, Part 3, p.51 and User Guidance, p.52). The transfer efficiency is 3% for painted wood (TNsG 2007, p.102) and dermal absorption of fludioxonil is 3%.

The amount of fludioxonil on the hands after repeated contact is given as: 0.0136 mg/cm² × 820 cm² × 0.2 × 0.03 = 0.067 mg
The amount of fludioxonil absorbed via the skin is: 0.067 mg × 0.03 = 0.00201 mg
Systemic dose of fludioxonil via skin = **3.3×10^{-5} mg/kg bw/day** (60 kg adult)

The total systemic dose via the inhalation and dermal routes is = **6.1×10^{-2} mg/kg bw/day**

Summary table: Secondary (indirect) exposures in professional workers				
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake (mg fludioxonil/kg bw/day)**	**Estimated dermal uptake (mg fludioxonil/kg bw/day)**	**Estimated total uptake (mg fludioxonil/kg bw/day)**
Scenario [PT7-20] **Sanding preserved paint or sealant**	**Tier I**	6.1×10^{-2}	3.3×10^{-5}	6.1×10^{-2}

8.4.2 Combined scenarios

Summary table: combined systemic exposure from professional uses			
Scenarios combined	**Estimated inhalation uptake**	**Estimated dermal uptake**	**Estimated total uptake**
Professionals – applying water-based paints by spraying (PT7-3), applying preserved mineral sealant or grout (PT7-5), and cleaning out spray equipment after use (PT7-7) – **Tier I**	$5.6x10^{-3}$	$2.3x10^{-2}$	$2.8x10^{-2}$
Professionals– applying water-based paints by spraying (PT7-3), applying preserved mineral sealant or grout (PT7-5), and cleaning out spray equipment (PT7-7) – **Tier II (IIa for PT7-3)**	$5.5x10^{-3}$	$5.1x10^{-3}$	$1.0x10^{-2}$
Professionals– applying water-based paints by spraying (PT7-3), applying preserved mineral sealant or grout (PT7-5), and cleaning out spray equipment (PT7-7) – **Tier II (IIb for PT7-3)**	$6.1x10^{-4}$	$5.1x10^{-3}$	$5.6x10^{-3}$
Professional– applying water-based paints using a brush or a roller (PT7-4), applying mineral sealant or grout (PT7-5), and washing out paint brushes (PT7-6) – **Tier I**	$2.3x10^{-4}$	$8.4x10^{-3}$	$1.1x10^{-2}$
Professional– applying water-based paints using a brush or a roller (PT7-4), applying mineral sealant or grout (PT7-5),) and washing out paint brushes (PT7-6) – **Tier II**	$2.3x10^{-3}$	$1.69x10^{-3}$	$3.9x10^{-3}$

Professional workers may carry out a number of tasks during a working shift where exposures to fludioxonil may arise. Combined exposures have been considered for the following scenarios:

- Professional workers – applying water-based paints by spraying (PT7-3), applying preserved mineral sealant or grout (PT7-5)and cleaning out spray equipment after use (PT7-7)
- Professional workers – applying water-based paints using a brush or a roller (PT7-4), applying preserved mineral sealant or grout (PT7-5) and washing out paint brushes after application (PT7-6)

8.5 NON-PROFESSIONAL EXPOSURE

This section considers exposures to fludioxonil which may occur in non-professionals (e.g. consumers) during the application of end-use products which have been preserved using Sporgard WB.

Non-professional exposure: preserved film products (PT7):

Non-professionals (amateurs/consumers) may be exposed to Sporgard WB and similar formulations when using preserved paints, sealants or grouts for DIY tasks. These products may be applied using a sprayer, a brush or a roller or an application tool such as a trowel depending on the application. Products are ready-mixed. After application, equipment may be cleaned. These products are preserved using Sporgard WB (containing up to 2% w/w fludioxonil) at concentrations up to 1.6% w/w giving a maximum fludioxonil concentration of 0.032% w/w in end use material (**Table IIB 3.1-1**).

The following tasks have been identified for consumers using preserved film products, PT7.

Mixing and loading (Sporgard WB exposure scenario):

Paints – mixing and loading is minimal

Application (Sporgard WB exposure scenario):

Spraying
Brush and roller
Applying sealants and grouts (mineral)

Post-application phase (Sporgard WB exposure scenario):

Cleaning out paint brushes after painting
Cleaning out spraying equipment after painting

Mixing and loading phase

The TNsG (2008) Excel Database on Human Exposure informs that ready-for-use paints containing film preservatives (PT 7) do not require mixing calculations because potential exposure arising during the mixing and loading phase are already accounted for in the default data for the application phase. This assumption is considered to also apply to consumers. Separate calculations for the mixing and loading phase have not therefore been carried out.

8.5.1 Scenario [PT7-8, PT7-9, PT7-10, PT7-11, PT7-12 and PT10-3] : Non-professional primary exposure scenarios

PT-7 Application phase – Spraying:

Description of Scenario [PT7-8] Spray application		
Non-professional applying preserved water-based paints by spraying Consumer Product Spraying and Dusting Model 3 – medium pressure spraying Task duration 40 min		
	Parameters[1]	**Value**
Tier 1	Potential hand exposure	176 mg/min (75th percentile)

	Potential dermal body exposure	120 mg/min (75th percentile)
	Indicative inhalation exposure	115 mg/m³ (75th percentile)
	Concentration of active ingredient	0.032%
	Duration of task	40 min/day
	Body weight	60
	Dermal absorption	3%

*please refer to footnote 7

Calculations for Scenario PT7-8]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-8]

Non-professionals (consumers) may be exposed to Sporgard WB when spraying water-based paint indoors using spraying equipment (e.g. using a hand-held electrically powered, DIY airless sprayer). Consumers may spray surfaces such as walls and ceilings and may be exposed to spills, contaminated equipment and by generated aerosol particulates. However, the generated particles are of large sizes because consumers will tend to use low pressured sprayers. The TNsG Part 3 (2002) p. 11 informs that consumers would typically carry out painting activities on 2 to 5 consecutive days, once a year. One application is made of duration 180 minutes per day. Potential exposure is via inhalation and dermal routes. However, it is expected that consumers will not carry out spray applications for periods longer than **40 minutes** as indicated in the TNsG Part 2 (2002) on page 78.

Note: an Ad hoc recommendation on model to be used for non-professional is now available (endorsed at WG III 2016) and could be used if refinement is need at product authorisation. The calculations in this CAR was made before the recommendation and therefore not taken into account.

Exposures to fludioxonil have been calculated for consumers applying end-use painting products indoors which have been preserved using Sporgard WB using Consumer product spraying Model 3: *"Non-professionals surface spraying (underside of joists with hand-held pressurised sprayer"* (TNsG 2002; Part 2, p199). The model describes a scenario in which 16 m^2 of rough wooden joists and the underside of floorboards are sprayed overhead, indoors with a water-based end-use product using a hand-held pressurised 3-litre sprayer. Although the model relates to the powered application of wood preservatives to joists and the underside of floorboards, according to the User Guidance 2002 (Annex 4) *Indicative exposure values*, this model is also considered to apply to other pump-pressured operations using a hand-held medium pressure sprayer and is therefore appropriate for assessing exposures to fludioxonil in consumers spraying paints and coatings which have been treated with Sporgard WB, to surfaces indoors. The model covers ready-to-use products and includes loading: a separate assessment for exposures during mixing and loading is not therefore required.

Taking into account moderate uncertainty in the underlying dataset, the 75th percentile indicative values[11] associated with the model have been used as follows (the figures in this model relate to actual skin measurement data so that no mitigation by clothes or gloves is appropriate):

Potential body exposure (legs, feet and face): 120 mg/min
Potential hand exposure(hands/forearms): 176 mg/min
Inhalation exposure: 115 mg/m^3

In Tier 1 it is assumed that no PPE is used. Thus, hand exposure is assessed on the basis of potential exposure values[7]. RPE is not worn by consumers.

The dermal absorption of fludioxonil is 3%. The concentration of fludioxonil in Sporgard WB used in the preservation of paints and coatings is 2% w/w. The maximum concentration of Sporgard WB in paints and coatings is 1.6% w/w.

PT-7 Application phase – Brush and roller:

Description of Scenario [PT7-9] Brush and roller application		
Non-professional applying preserved water-based paints using a brush or roller ConsExpo model v.4.1 and default scenario for Brush/roller painting, waterborne wall paint (RIVM Painting Products Factsheet p. 28): Inhalation exposure: ConsExpo model: "Exposure to vapour" (Release mode: Evaporation; evaporation from increasing area) Dermal exposure: ConsExpo model: "Constant rate"		
	Parameters	**Value**
Tier I	Vapour pressure fludioxonil	3.9 x 10^{-7} Pa
	Molecular weight fludioxonil	248.2 g/mol
	Concentration of active ingredient	0.032%
	Inhalation exposure	
	Exposure duration	132 minutes
	Application duration	120 minutes
	Product amount	3500 g
	Room volume	20 m^3
	Ventilation rate	0.6 h^{-1}
	Release area	15 m^2
	Temperature	20°C

11 The indicative data in the TNsG are presented as potential hand/forearm exposure and therefore it is assumed that no gloves were worn. The indicative hand value indicates a high level of dermal despostion so it is unlikely that the study data were based on gloves being worn (however it has not been possible to locate the orignal study data „HSL 2001" to confirm this.

	Mass transfer rate	Thibodeaux
	Molecular weight matrix	120 g/mol
	Inhalation rate	1.25 m^3/hr
	Uptake fraction	100%
	Adult body weight	60 kg
	Dermal exposure	
	Contact rate	30 mg/min
	Release duration	120 minutes
	Dermal absorption	3%

Calculations for Scenario PT7-9]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-9]

Consumers may be exposed to Sporgard WB when applying water-based paint indoors using a brush or roller. Potential exposure is via the inhalation and dermal routes. Due to their specialised nature, consumers are not expected to work with these products occasionally (i.e. 1 or 2 times a year only).

Exposures have been assessed using the ConsExpo model v.4.1 and the corresponding parameters for the default scenario: Brush/roller painting, waterborne wall paint, provided in the RIVM Painting Products Factsheet Section 2.6, p. 28. The scenario describes the brushing or rolling of two walls in a small room with low ventilation.

Exposures have been assessed using the ConsExpo model v.4.1 and the corresponding parameters for the default scenario: Brush/roller painting, waterborne wall paint, provided in the RIVM Painting Products Factsheet Section 2.6, p. 28. The scenario describes the brushing or rolling of two walls in a small room with low ventilation.

Inhalation exposure during the painting task (and clean-up) was assessed using the ConsExpo model: "Exposure to vapour", set in the evaporation (evaporation from an increasing area) mode of release. The room size and ventilation rates are assumed to be 20 m^3 and 0.6 h^{-1}, respectively, based on an unspecified room. For painting two walls of a total surface area of 15 m^2, it is assumed that 2.5 Litres of paint will be used. Based on a paint density of 1.4 g/cm^3 (Applicant information), the amount of paint product applied would be 3500 g. It is assumed that after painting, the room is cleaned up and left afterwards. The exposure duration of 132 minutes is therefore set at 1.1 times the application duration of 120 minutes to account for the clean-up time. The Thibodeaux method has been used to determine the mass transfer rate since this is the default approach for waterborne systems. The molecular weight matrix has been set at 120 g/mol: the default for waterborne systems of unknown composition. Inhalation exposure was determined as internal dose on the day of exposure (e.g. the absorbed dose per kg bodyweight during one day in mg/kg bw/day)

Dermal exposure during the painting task was determined using the ConsExpo "Constant rate" direct contact model. The contact rate has been assumed to be 30 mg/min: the default rate during the brushing

and rolling of painting products, (downward painting and painting directed to the side; RIVM Painting Products Factsheet p. 24). Dermal exposure was determined as the internal dose on the day or exposure (e.g. the absorbed dose per kg bodyweight during one day).

In the Tier 1 assessment it is assumed that no PPE is used.

The dermal absorption of fludioxonil is 3%. The concentration of fludioxonil in Sporgard WB used in the preservation of paints and coatings is 2% w/w. The maximum concentration of Sporgard WB in paints and coatings is 1.6% w/w, giving a maximum fludioxonil concentration of 0.032% w/w in end use material.

PT-7 Application phase: - Applying mineral sealants and grouts

Description of Scenario [PT7-10] Applying preserved mineral sealant or grout		
Non-professional applying preserved mineral sealant or grout ConsExpo model v.4.1 and default scenario for joint sealant (RIVM DIY Products Factheet p. 59) Inhalation exposure: ConsExpo model: "Exposure to vapour" (Release mode: Evaporation; evaporation from increasing area) Dermal exposure: ConsExpo model: "Constant rate"		
	Parameters	**Value**
Tier 1	Vapour pressure fludioxonil	3.9×10^{-7} Pa
	Molecular weight fludioxonil	248.2 g/mol
	Concentration of active ingredient	0.032%
	Inhalation exposure	
	Exposure duration	45 minutes
	Application duration	30 minutes
	Product amount	75 g
	Room volume	10 m^3
	Ventilation rate	2 h^{-1}
	Release area	250 cm^2
	Temperature	20°C
	Mass transfer rate	Langmuir
	Molecular weight matrix	3000 g/mol
	Inhalation rate	1.25 m^3/hr
	Adult body weight	60 kg
	Dermal exposure	
	Contact rate	50 mg/min
	Release duration	30 minutes
	Dermal absorption	3%

Calculations for Scenario (PT7-10)

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-10]

Consumers may be exposed to fludioxonil when using preserved mineral sealants or grouts for DIY tasks. These end-use products are typically supplied in ready-mixed formulations in tubs or other containers. Using a trowel or scraper, they may be applied to surfaces directly from their containers as thick pastes which dry over time (i.e. they are not powder type products which require mixing with water prior to use). No mixing and loading or post-application clean-up is required. Potential exposure may occur via the dermal route (i.e. as contamination of hands during the application of product) but is expected to be minor as the products would usually be handled using an application tool. Inhalation exposures are unlikely, but have nevertheless been considered in a worst case approach. Consumers as expected to carry out such tasks infrequently, i.e. once or twice a year.

Exposures have been assessed using the ConsExpo model v.4.1 and the corresponding parameters for the default scenario: Joint sealant provided in the RIVM DIY Products Factsheet Section 4.1.1, p. 59. The scenario describes the application of a joint sealant in a bathroom, where the joints between a bathtub, shower cabinet or washstand and wall will be sealed off. While this scenario does not specifically address the use of a mineral sealant product (the scenario typically reflect the application of a silicon sealant), the information provided in the RIVM DIY Products Factsheet is detailed and relevant to use scenarios by consumers.

Inhalation exposure during the task was assessed using the ConsExpo model "Exposure to vapour", set in the evaporation (evaporation from an increasing area) mode of release. The total joint length between a bathtub and wall is estimated to be 5 metres and requires 75 ml of sealant. Assuming the density of the sealant is 1 g/cm^3, the amount of product used will be 75g. The default application duration is 30 minutes and the total exposure time is 45 minutes, allowing for finishing off and cleaning. The default values for the volume of the bathroom and the ventilation rate respectively are: 10 m^3 and 2 hr^{-1}. The release area is 250 cm^2; determined as a strip of sealant 5 m long and 5 mm wide. The Thibodeaux method has been used to determine the mass transfer rate since this is the default approach. The molecular weight matrix has been set at 3000 g/mol: the default for DIY products. Inhalation exposure was determined as the internal dose on the day of exposure (e.g. the absorbed dose per kg bodyweight during one day).

Dermal exposure was determined using the ConsExpo "Constant rate" direct contact model. It is assumed that exposure will be to the fingertips only when used to smoothen down the applied sealant (skin surface area = 2 cm^2). The contact rate has been assumed to be 50 mg/min: the dermal load is expected to be significant (1.5 g divided by the release duration of 30 minutes).Dermal exposure was determined as the internal dose on the day or exposure (e.g. the absorbed dose per kg bodyweight during one day

In the Tier 1 assessment it is assumed that no PPE is used.

The dermal absorption of fludioxonil is 3%. The concentration of fludioxonil in Sporgard WB used in the preservation of mineral sealants and fillers is 2% w/w. The maximum concentration of Sporgard WB in mineral sealants and fillers is 1.6% w/w giving a maximum fludioxonil concentration of 0.032% w/w in end use material.

PT-7 Post-application phase: Washing out paint brushes

Description of Scenario [PT7-11] **Washing out paint brushes**		
Non-professional washing out paint brushes after application HEEG opinion 2008		
	Parameters	**Value**
Tier 1	Brush size: 10 x 10 x 2 cm (large brush, worst case)	200 ml
	Volume of paint remaining in brush after painting	1/8 of brush size = 25 ml
	Density of water-based paint	1.4 g/mL
	Volume of each washing solution:	at least 400 ml
	Percentage of residues remaining in brush after each washing step:	10%
	Following each washing step, percentage of residues squeezed out of brush:	50%
	Percentage of residues squeezed out of brush which are absorbed by the cloth:	90%
	Concentration of active ingredient	0.032%
	Body weight	60
	Dermal absorption	3%

Calculations for Scenario PT7-11]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-11]

Consumers may be exposed when washing out brushes after painting tasks and cleaning out spray equipment. The same approaches as described for professionals have been used to assess exposures (e.g. HEEG washing brushes model and BEAT cleaning out spray equipment).

PT-7 Post-application phase - Cleaning of spray equipment

Description of Scenario [PT7-12] **Spray equipment cleaning**		
Non-professional cleaning out spray equipment after application[2] BEAT indicative data Task duration 30 min		
	Parameters	**Value**
Tier I	Potential hands exposure	50.1 mg/min (75th percentile)*
	Potential dermal body exposure	26.9 mg/min (75th percentile)*
	Indicative inhalation exposure	Neglible
	Concentration of active ingredient	0.032%

	Duration of task	30 min/day
	Body weight	60
	Dermal absorption	3%

**values corrected for the density of preserved paints

Calculations for Scenario [PT7-12]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario *[PT7-12]*
Consumers may be exposed when washing out brushes after painting tasks and cleaning out spray equipment. The same approaches as described for professionals have been used to assess exposures (e.g. HEEG washing brushes model and BEAT cleaning out spray equipment).

PT-9 Non-professional exposure: preserved materials (PT9)

Non-professional uses are not envisaged for preservatives used to treat industrial paper (PT9.02) as the use involves incorporation into articles during the formulation/manufacturing stage. The potential for secondary exposure has been addressed separately.

PT-10 Application phase: - cutting/sawing or drilling gypsum drywall[1]

Description of Scenario [PT10-3] cutting/sawing or drilling gypsum drywall[1]		
Non-Professional cutting/sawing or drilling gypsum drywall[1] ECETOC TRA V3 model – workers 1 hour per day		
	Parameters[1]	**Value**
Tier 1	Concentration of active ingredient	0.032%
	Duration of task	60 minutes per day
	Default value dermal exposure	2.83 mg/kg bw/day
	Default value inhalation exposure	0.6 mg/m^3
	External day dose for a 70 kg person	198 mg/day
	Dermal absorption	3%

[1]Oral exposure is not considered relevant

Calculations for Scenario (PT10-3)

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT10-3]
Non-professionals (consumers) may be exposed to fludioxonil when using drywall products containing gypsum power which has been treated with Sporgard WG to prevent fungal growth. Consumers may use power tools to cut, saw or drill drywall during DIY construction tasks.
Sporgard WG is incorporated as a preservative in gypsum powder at concentrations up to 1.6%, giving maximum concentrations of fludioxonil of 0.032% w/w (based on a fludioxonil concentration of 2% w/w).

The following tasks have been identified for consumers using preserved masonry products, PT10.

Application
Cutting, sawing or drilling drywall during construction tasks using power tools
This scenario is described in more detail below.

Application phase
Consumers may be exposed to fludioxonil when cutting, sawing or drilling drywall products preserved using Sporgard WG, for example when carrying out DIY tasks. These processes may generate dusts of the treated gypsum powder which is held together by the paper coating. Consumers may be exposed to the dust by inhalation or dermal contact. There are no data available on the duration of time consumers spend carrying out such tasks. As a worst case scenario it is assumed consumers spent up to **1 hour per day** working with drywall products. Consumers are expected to carry out such tasks infrequently.
There are no models or data available in the TNsG to assess potential exposures in consumers arising from the cutting, sawing or drilling of drywall products. As a worst case scenario exposures have been assessed using a similar approach as for workers discussed in Section IIB 3.2.2.3 (i.e. using the default data in the ECETOC Targeted Risk Assessment (TRA) model version, adapted for a shorter exposure durations of up to 1 hour). While this model provides a screening level assessment of exposures for the purposes of assessing the potential health risks of chemicals in workers which is likely to overestimate exposures in consumers, it has nevertheless been used to provide a worst-case exposure assessment.
Default data are provided for the scenario: high mechanical energy work-up of substances bound in materials and/or articles (e.g. grinding, mechanical cutting, drilling or sanding).
Exposure is predominately expected to be to dust. Dermal exposures are to hands. Consumers would not be expected to wear gloves; hence exposures have been assessed at the Tier 1 level only. Default values for these tasks carried out indoors (without the uses of any local exhaust ventilation), for up to 1 hour /day are **2.83 mg/kg bw/day** and **0.6 mg/m^3** for dermal and inhalation exposures respectively. The external day dose of gypsum powder is assumed to **198 mg/day** (the ECETOC TRA assumes an adult has a bodyweight of 70 kg; the external dose used in the calculation = 70 kg x 2.83 mg/kg bw/day).

Summary table: systemic exposure from non-professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake (mg fludioxonil/kg bw/day)**	**Estimated dermal uptake (mg fludioxonil/kg bw/day)**	**Estimated oral uptake[1]**	**Estimated total uptake (mg fludioxonil/kg bw/day)**
Application phase					
Scenario [PT7-8] **Spray application**	Tier 1 (no PPE)	5.1×10^{-4}	1.9×10^{-3}	Not relevant	2.4×10^{-3}
Scenario [PT7-9] **Brush and roller application**	Tier 1 (no PPE)	1.9×10^{-10}	5.8×10^{-4}	Not relevant	5.8×10^{-4}
Scenario [PT7-10] **Applying preserved mineral sealant or grout**	Tier 1 – (no PPE)	8.7×10^{-9}	2.4×10^{-4}	Not relevant	2.4×10^{-4}
Scenario [PT10-3] **Cutting/sawing**	Tier 1 (no PPE)	4.0×10^{-6}	3.2×10^{-5}	Not relevant	3.6×10^{-5}
Post-application phase					
Scenario [PT7-11] **Wash out paint brush**	Tier 1 – (no PPE)	Negligible	2.8×10^{-5}	Not relevant	2.8×10^{-5}
Scenario [PT7-12] **Spray equipment cleaning**	Tier 1 (no PPE)	Negligible	3.7×10^{-4}	Not relevant	3.7×10^{-4}

[1] *Oral exposure is not considered relevant for consumers/non-professionel*

Scenario [PT7-21] : Non-professional exposure scenario

Description of Scenario [PT7-21] Adult (Non-professional) – Removing preserved paint or sealant by sanding		
Secondary (indirect): Non-professional (i.e. consumer) removes preserved paint or sealant by sanding. Task duration- 1 hrs per day (acute exposure scenario)		
	Parameters	**Value**
Tier 1	Concentration of active substance	0.032% w/w
	Density of paint	1.4 g/ml
	Concentration of active in dried paint	0.058% w/w
	Inhalation exposure	
	Active substance concentration in 0.1 cm paint layer	0.815 mg/cm^3
	Inhalation rate (intensive activity)	3 m^3/hr
	Task duration	1 hr
	Exposure to wood dust during sanding for 60 minutes	100 mg/m^3
	Density of soft wood	0.4 g/cm^3
	Adult bodyweight	60 kg
	Dermal exposure	
	Highest active substance concentration on painted surface	0.0136 mg/cm^2
	Surface area of both hands	820 cm^2
	Fraction of hands contaminated during prolonged contact	20%
	Transfer efficiency for painted wood	3%
	Dermal absorption	3%
	Adult bodyweight	60 kg

Calculations for Scenario (PT7-21)

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-21]

Non-professionals (i.e. consumers) may be indirectly exposed to fludioxonil when removing paint from surfaces which have been painted using a product preserved using Sporgard WB or when removing a preserved sealant by sanding. Inhalation and dermal exposures to dust generated during the sanding process is expected to occur. Exposures during the removal of a sealant are not expected to be any higher that those following the removal of paint. In this case, the assessment will also cover the removal of the sealant by sanding and separate calculations will not be presented. It is assumed that the consumer, may be perform such sanding operations occasionally, for up to 1 hour in a day, such that this can be considered as an acute exposure scenario. As a worst-case scenario, it is assumed that sanding is carried out manually. Consumers would not be expected to wear any protective gloves when sanding.

Inhalation exposure

In this scenario, it is assumed that a non-professional (i.e. a consumer) is sanding a painted surface and the active substance, fludioxonil, is in a paint layer of thickness 0.1 cm. It is assumed that sanding takes 1 hour. Taking into account a concentration of fludioxonil in wet paint of 0.032 % w/w, a paint density of 1.4 g/ml, and a 1.82 factor for the higher concentration of active substance in dried paint (Applicant information), the active substance concentration in 0.1 cm paint layer which is sanded is 0.815 mg/cm^2.

As a conservative assumption, according to air measurements made during paint sanding operations in a joinery shop made by the Finnish Institute of Occupational Health (number of measurements 80, arithmetic mean 13 mg/m^3, median 6.3 mg/m^3, range 0.3-81 mg/m^3), during one hour of sanding, a worker would be exposed to wood dust at a concentration of 100 mg/m^3 (Measurement results publised in: Liukkonen T, Korhonen K, Lindroos L, Nylund L. Puusepänteollisuuden ke-mikaaliselvitys. Raporttisarja 4. Lappeenrannan aluetyöterveyslaitos, Lappeenranta 1992. 49 s + liitteet. ISBN 951-801-928-2, Liukkonen T, Korhonen K, Lindroos L. Kemikaalit ja niille altistuminen puusepänteollisuudessa. Työ ja ihminen 9:55-66 (1995). As a worst-case approach, this value for the exposure to wood dust duing sanding has been considered for a consumer. It is expected that manual sanding is a more intensive activity that normal DIY tasks for which a default inhalation rate of 1.25 m^3/hour (light exercise) is assumed. A more representative inhalation rate is assumed to be 3 m^3/hr. The amount of dust inhalation would be: 3 m^3/h x 1 h x 100 mg/m^3 = 300 mg. Based on a density of soft wood of 0.4 g/cm^3, the volume of dust inhaled would be: (300 mg/1000)/0.4 g/cm^3 = 0.75 cm^3. The amount of fludioxonil in the wood dust is therefore calculated as: 0.815 mg/cm^3 x 0.75 cm^3 = 0.61152 mg. The systemic inhalation dose of fludioxonil for a professional worker of bodyweight 60 kg is determined as **1.0 x 10^{-2} mg/kg bw/day**.

As an alternative approach, a reverse reference scenario was used to determine an estimate of the maximum amount of exposure that might be acceptable. The short-term AEL-value of 1 mg/kg bw/day was used to calculate the amount of product that would lead to that amount by inhalation. The inhalation rate is assumed to be 3 m^3/h and the task duration is 1 hours. The concentration of fludioxonil in dried paint is 0.058% w/w (i.e. 1.82 times the concentration in wet paint).

The amount of fludioxonil in the paint dust: 0.59 mg/kg /day × 60 kg = 35.4 mg/day
The amount of paint (i.e. sanding dust): 35.4 mg/day ÷ 0.058% = 60782 mg/day.

The amount of air inhaled during the task: 3 m^3/h × 1h = 3 m^3

Hence the concentration of sanding dust in the inhaled air is = 60782 mg ÷ 3 m^3 = 20261 mg/m^3

According to measurements of air concentration after paint sanding operations in a joinery shop made by the Finnish Institute of Occupational Health, this is 250 times greater than the maximum measurement result (number of measurements 80, arithmetic mean 13 mg/m^3, median 6.3 mg/m^3, range 0.3-81 mg/m^3).

Dermal exposure (hands – no gloves worn)

The highest concentration of fludioxonil on the preserved surface is determined to be 0.136 mg a.s./cm² (According to the RIVM Painting Products Factsheet, 2.5 L of paint would be applied to walls of a total surface area of 15 m^2, such that the application rate for paint is 0.01667 ml/cm^2. Accounting for a paint density of 1.4 g/ml and that dried paint contains fludioxonil at 0.058 % w/w, the concentration of the active substance in dried paint on the treated surface is 0.0136 mg a.s./cm^2).

The surface area of both hands is 820 cm² and during prolonged and repeated contact, 20% of the hand is contaminated (TNsG 2002, Part 3, p.51 and User Guidance, p.52). The transfer efficiency is 3% for painted wood (TNsG 2007, p.102) and dermal absorption of fludioxonil is 3%.

The amount of fludioxonil on the hands after repeated contact is given as: 0.0136 mg/cm² × 820 cm² × 0.2 × 0.03 = 0.067 mg
The amount of fludioxonil absorbed via the skin is: 0.067 mg × 0.03 = 0.00201 mg
Systemic dose of fludioxonil via skin = **3.3×10^{-5} mg/kg bw/day** (60 kg adult)

The total systemic dose via the inhalation and dermal routes is = **1.0×10^{-2} mg/kg bw/day**

Summary table: Secondary (indirect) exposures in non-professionals				
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake (mg fludioxonil/kg bw/day)**	**Estimated dermal uptake (mg fludioxonil/kg bw/day)**	**Estimated total uptake (mg fludioxonil/kg bw/day)**
Scenario [PT7-21] **Sanding preserved paint or sealant**	**Tier I**	1.0×10^{-2}	3.3×10^{-5}	1.0×10^{-2}

8.5.2 Combined scenarios

Summary table: Combined systemic exposure from Non-professional uses			
Scenarios combined	**Estimated inhalation uptake (mg fludioxonil/kg bw/day)**	**Estimated dermal uptake (mg fludioxonil/kg bw/day)**	**Estimated total uptake (mg fludioxonil/kg bw/day)**
Non-professionals – applying water-based paints by spraying (PT7-8), applying preserved mineral sealant or grout (PT7-10), and cleaning out spray equipment after use (PT7-12) – Tier I	5.1×10^{-4}	2.2×10^{-3}	2.7×10^{-3}

Non-professionals – applying water-based paints using a brush or a roller (PT7-9), applying preserved mineral sealant or grout (PT7-10) and washing out paint brushes after application (PT7-11) – Tier I	$8.9x10^{-9}$	$8.5x10^{-4}$	$8.5x10^{-4}$

Non-professionals (consumers) may carry out a number of tasks in a day where exposures to fludioxonil may arise, for example when conducting DIY activities. Combined exposures have been considered for the following scenarios:

- Non-professionals – applying water-based paints by spraying (PT7-8), applying preserved mineral sealant or grout (PT7-10), and cleaning out spray equipment after use (PT7-12)
- Non-professionals – applying water-based paints using a brush or a roller (PT7-9), applying preserved mineral sealant or grout (PT7-10) and washing out paint brushes after application (PT7-11)

8.6 SECONDARY EXPOSURE OF THE GENERAL PUBLIC EXCLUDING DIETARY EXPOSURE

Potential indirect exposure to general public is considered below for each product type

8.6.1 Scenario [PT7-13, PT7-14, PT7-15, PT7-16 and PT7-17]

Potential indirect exposure is most likely to occur via inhalation of volatile components from freshly painted surfaces following use. Fludioxonil has low volatility; hence inhalation of vapours is unlikely.

Potential indirect exposures to fludioxonil from products (PT7) preserved using Sporgard WB may arise during the following acute and chronic scenarios:

- Child/adult touching a wet or dry painted surface
- An adult washing out contaminated coveralls
- Child/adult touching the preserved materials (e.g. mineral sealants or fillers)

These scenarios are described in more detail below.

Scenario PT7-13, PT7-14, PT7-15 & PT7-16 (acute exposure):

a) **Toddler – touching wet painted surface (PT7-13)**
b) **Toddler – touching wet painted surface and mouthing (PT7-14)**
c) **Toddler – touching dry painted surface (PT7-15)**
d) **Toddler – touching dry painted surface and mouthing (PT7-16)**

Touching painted surface

Non-users, for example a child or an adult, may be exposed to fludioxonil when touching a painted surface before the paint (preserved with Sporgard WB) has dried or when touching dried paint on a painted surface.. . Since this scenario is more critical for children due to their lower bodyweight, an assessment has been carried out for a toddler as defined by the HEEG *Opinion on Default human factors values for use in exposure assessments for biocidal products* (2013): i.e. a child aged between 12 and 36 months with unsteady walking and a bodyweight of 10 kg, and covers exposures in adults also. Exposures have been considered via the dermal route and via the oral route (e.g. from mouthing contaminated hands).

Exposures to fludioxonil in toddlers when touching wet or dried paint have been assessed using the approach set out in Recommendation No. 5 of the Biocidal Product Committee Ad hoc Working Group on Human Exposure: Non-professional use of antifouling paints: exposure assessment for a toddler (as agreed at the Human Health Working Group I on 28 January 2015 (referred to as HEAdhoc Recommendation no. 5). This approach is described further below.

PT7-13 Toddler – dermal contact with wet paint

Description of Scenario [PT7-13] Toddler – dermal contact with wet paint		
Secondary (indirect): Toddler touches a wet painted surface. Approach: Recommendation No. 5 of the BPC Ad hoc Working Group on Human Exposure: Non-professional use of antifouling paints: exposure assessment for a toddler		
	Parameters	**Value**
Tier 1	Application rate for paint (non-professional application)	0.0167 ml paint/cm^2

Calculations for Scenario [PT7-13]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-13]

It is assumed that a toddler touches a wet painted surface after the application of paint treated with Sporgard WG once. The paint, with contains Sporgard WG at a concentration of 1.6% (giving a concentration of fludioxonil in the wet paint of 0.032% w/w) is applied by a non-professional (i.e. a consumer) in a domestic setting using a brush and a roller, and 2.5 L of paint is applied to a two walls of total surface area of 15 m^2 (default for brush and roller scenario provided in the RIVM Painting Products Factsheet p.28). The application rate of the product is therefore calculated as 0.0167 ml paint/cm^2 and the density of the paint is 1.4 g/ml.

Taking into account that it is unlikely that 100% of the wet paint from the treated surface will transfer to the toddler's hands, the transfer coefficient of paint from the treated surface to the hands is 50% (default value provided in HEAdhoc Recommendation no. 5). The surface area of the toddler's hands in contact

with the wet painted surface is 115.2 cm^2 (i.e. the palms only of both hands). The bodyweight of a toddler is 10 kg (HEEG Opinion agreed at TMII 2013). The dermal absorption of fludioxonil is 3%.

PT7-14 Toddler – dermal contact with wet paint and mouthing

Description of Scenario [PT7-14] Toddler – dermal contact with wet paint and mouthing		
Secondary (indirect): Toddler touches a wet painted surface and mouths contaminated hands. Approach: Recommendation No. 5 of the BPC Ad hoc Working Group on Human Exposure: Non-professional use of antifouling paints: exposure assessment for a toddler		
	Parameters	**Value**
	Application rate for paint (non-professional application)	0.0167 ml paint/cm^2
Tier 1	Concentration of active ingredient in wet paint	0.032%
	Density of wet paint	1.4 g/ml
	Toddler bodyweight	10 kg
	Dermal exposure	
	Transfer coefficient of wet paint from treated surface to hand	50%
	Total area of toddler hands in contact with the removed wet paint	115.2 cm^2
	Dermal absorption of fludioxonil	3%
	Oral exposure	
	Transferrable fraction of wet paint from hand to mouth (i.e. from two fingers)	10%
	Oral absorption of fludioxonil	100%

Calculations for Scenario [PT7-14]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-14]

In this scenario, it is assumed that a toddler touches a wet painted surface (as described for Scenario PT7-13) and mouths their contaminated hands. Dermal exposures have been determined as described previously for scenario PT7-13. According to HEAdhoc Recommendation no. 5, it is unlikely that a toddler will lick all the wet paint from its hands but is more likely that two fingers will be sucked. Two fingers from one hand constitute about 10% of the total area of both hands, hence the transferable fraction of paint from the hands to the mouth is taken as 10%. The oral absorption of fludioxonil is 100%.

PT7-15 Toddler – dermal contact with dry paint

Description of Scenario [PT7-15] Toddler – dermal contact with dried paint
Secondary (indirect): Toddler touches a dried painted surface. Approach: Recommendation No. 5 of the BPC Ad hoc Working Group on Human Exposure: Non-professional use of antifouling paints: exposure assessment for a toddler

	Parameters	Value
Tier 1	Application rate for paint (non-professional application)	0.0167 ml paint/cm^2
	Concentration of active ingredient in dried paint	0.058%
	Density of wet paint	1.4 g/ml
	Toddler bodyweight	10 kg
	Dermal exposure	
	Transfer coefficient of dried paint from treated surface to hand	3%
	Total area of toddler hands in contact with the removed dried paint	46.08 cm^2
	Dermal absorption of fludioxonil	3%

Calculations for Scenario [PT7-15]

Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-15]

It is assumed that toddler touches a dried painted surface after the application of paint treated with Sporgard WG once. The paint, with contains Sporgard WG at a concentration of 1.6% (giving a concentration of fludioxonil in the wet paint of 0.032% w/w) is applied by a non-professional (i.e. a consumer) in a domestic setting using a brush and a roller, and 2.5 L of paint is applied to a two walls of total surface area of 15 m^2 (default for brush and roller scenario provided in the RIVM Painting Products Factsheet p.28). The application rate of the product is therefore calculated as 0.0167 ml paint/cm^2 and the density of the paint is 1.4 g/ml. The concentration of fludioxonil in dried paint is expected to be higher than that in wet paint, as solvents/carriers evaporate on drying. The concentration of the active substance in dried paint is expected to be 1.82 times greater than that in wet paint (i.e. 0.058% w/w versus 0.032% w/w; information from Applicant).

The transfer coefficient of dried paint from the surface to the hand is 3% (default value provided in HEAdhoc Recommendation No. 5). Following single hand press contacts onto a powder-loaded glass plate about 40% of the palm of the hand was exposed. Hence, the surface area of the toddler's hands in contact with the wet painted surface is 46.08 cm^2: 40% of the palm of both hands (115.2 cm^2). The bodyweight of a toddler is 10 kg (HEEG Opinion agreed at TMII 2013). The dermal absorption of fludioxonil is 3%.

PT7-16 Toddler – dermal contact with dry paint and mouthing

Description of Scenario [PT7-16] Toddler – dermal contact with dried paint and mouthing		
Secondary (indirect): Toddler touches a dried painted surface and mouths contaminated hands Approach: Recommendation No. 5 of the BPC Ad hoc Working Group on Human Exposure: Non-professional use of antifouling paints: exposure assessment for a toddler		
	Parameters	**Value**
Tier 1	Application rate for paint (non-professional application)	0.0167 ml paint/cm^2

	Concentration of active ingredient in dried paint	0.058%
	Density of wet paint	1.4 g/ml
	Toddler bodyweight	10 kg
	Dermal exposure	
	Transfer coefficient of dried paint from treated surface to hand	3%
	Total area of toddler hands in contact with the removed dried paint	46.08 cm^2
	Dermal absorption of fludioxonil	3%
	Oral exposure	
	Transfer coefficient of dried paint from hands to mouth	50%
	Oral absorption of fludioxonil	100%

Calculations for Scenario [PT7-16]
Detailed calculations can be seen in Appendix II.

Further information and considerations on scenario [PT7-16]

In this scenario, it is assumed that a toddler touches a dried painted surface (as described for Scenario PT7-15) and mouths their contaminated hands. Dermal exposures have been determined as described previously for scenario PT7-15. According to HEAdhoc Recommendation No. 5, the transferrable fraction of dried paint from the hand to the mouth is 50%. The oral absorption of fludioxonil is 100%.

Scenario PT7-17 (medium term exposure):

Adult cleaning work clothes at home - washing out contaminated overalls

Indirect, secondary exposures to fludioxonil may arise when adults are washing out contaminated coveralls after spraying paint which contains Sporgard WB as a preservative (e.g. after 5 days of use). The worst-case scenario for exposure is via the dermal route, mainly to the hands from handling the contaminated clothing prior to their introduction into the washing machine. Contamination of a coverall is predicted to be highest for workers spraying articles with the end-use product. The indicative value for the body of **365.4 mg/min** is used in the respective exposure assessment (value from BEAT transformed via the paint density). Given the duration of the process of **360 minutes/day**, it can be calculated that contamination on coveralls would be 365.4 mg/min × 360 min = 131544 mg in-use product/day = 42.09 mg fludioxonil/day (in-use formulation contains 0.032% w/w fludioxonil). It is assumed that the coverall is washed weekly, after 5 days' wear. Therefore, following 5 days' wear, the total maximum residues accumulated on the coverall would be:

5 days × 42.09 mg fludioxonil/day = 210.47 mg fludioxonil/week

It is assumed that the total outer surface area of a medium sized coverall is 22.700 cm² therefore, expressed as mg a.s./cm² of coverall; the accumulated residue would be 9.3 x 10^{-3} mg a.s./cm².

For an adult, the total area of both hands (front and back) is 820 cm² (HEEG Opinion on *Default human factors for use in exposure assessments for biocidal products,* 2013). It is expected that the task will be performed with dry hands. The transfer coefficient for contamination (dried fluid) from cotton, knitwear to dry hands is 20% (TNsG 2007, p. 102) with fludioxonil displaying a dermal penetration of 3%. The systemic dose for a 60 kg adult can be calculated as:

Fludioxonil residues on coverall x hand surface area x transfer coefficient x dermal absorption]/ bodyweight = [9.3 x 10^{-3} mg a.s./cm^2 x 820 cm^2 x 0.2 x 0.03] / 60 **= 7.6 x 10^{-4} mg/kg bw/day**

Scenario PT7-18 & PT7-19 (medium term exposure): Toddler-dermal contact with preserved materials (e.g. mineral sealants and fillers)

a) Toddler –dermal contact with wet preserved material (PT7-18)

b) Toddler – dermal contact with wet preserved material and mouthing (PT7-19)

Mineral sealants and fillers dry hard and therefore indirect exposures to fludioxonil in this case is unlikely. However, non-users, for example a child or an adult, may be exposed to fludioxonil when touching preserved mineral sealants or fillers before they have dried. Since this scenario is more critical for children due to their lower bodyweight, an assessment has been carried out for a toddler as defined by the HEEG *Opinion on Default human factors values for use in exposure assessments for biocidal products* (2013): i.e. a child aged between 12 and 36 months with unsteady walking and a bodyweight of 10 kg, and covers exposures in adults also. A scenario is assumed where a toddler may be playing in a room after the application of these end-use products, for example a bathroom where tiles have been grouted. Exposures have been considered via the dermal route and via the oral route (e.g. from mouthing contaminated hands).

a) Toddler –dermal contact with wet preserved material (PT7-18)

A toddler (10 kg) touches applied wet mineral sealants or fillers once. It is assumed that the total surface area of the palms hands area of a toddler is cm^2 (HEEG value for the palms of two hands) with 20 % of the hands area exposed. The concentration of fludioxonil in the mineral sealant is 0.032 % (end-use products contain 1.6% Sporgard which contains 2% fludioxonil). A transfer coefficient of 20% (in line with the TNsG, 2007, p. 102) is assumed as worst-case scenario for mineral sealants. The film thickness from which fludioxonil can be transferred on the hands is assumed to be 100 µm (default value of 0.01 cm, TGD on Risk Assessment, part 1, p. 223). A density of the mineral sealant of 1.0 g/mL is assumed.

The amount of mineral sealants transferred to the child's hands would be given as:

Mineral sealants dislodged = 0.2 x 100 cm^2 x 0.01 cm x 1.0 g/mL = 0.2 g.

For mineral sealants containing Sporgard WB at concentrations up to 1.6 % w/w, the amount of biocidal product transferred to the hands would be:

Biocidal product transferred to hands = 0.2 g x 1.6/100 x 1000 = 3.2 mg.

Sporgard WB contains 2% w/w fludioxonil. Assuming the toddler has a body weight of 10 kg and the dermal absorption value is 3%, the systemic dose of fludioxonil (mg/kg bw/day) is calculated as:

Systemic dose of fludioxonil via dermal exposure =

[3.2 mg x (2/100) x (3/100)] / 10 kg = **1.9×10^{-4} mg/kg bw/day** (10 kg toddler)

b) Toddler – dermal contact with wet preserved material and mouthing (PT7-19)

In addition to dermal uptake, oral uptake from hands by licking is considered. The systemic dose via the dermal route has been derived in the previous section as 2.16×10^{-4} mg/kg bw/day. It is assumed that 10% of the calculated external dermal dose of fludioxonil (3.6 mg x (2/100) = 0.072 mg) is ingested by the toddler via hand-to-mouth contact. Assuming absorption via the oral route is 100%, the systemic oral dose will be:

Systemic dose of fludioxonil via oral exposure =

(0.072 mg x 0.1) / 10 kg = **7.2×10^{-4} mg/kg bw/day** (10 kg toddler)

The total systemic dose is therefore given as the sum of the doses via the dermal and oral routes = $2.2 \times 10^{-4} + 7.2 \times 10^{-4} = 9.4 \times 10^{-4}$ mg/kg bw/day (10 kg toddler)

Scenario (Chronic exposure) – Inhalation of volatilised residues indoors.

Long-term inhalation exposure to volatilised residues of fludioxonil has been estimated using the Tier 1 Screening approach in the HEEG Opinion No. 13 on: ***Assessment of inhalation exposure of volatilised biocides active substance*** (Endorsed at TM IV 2011 and amended after TM III 2103 to take into account changed default human factor values).

To determine whether inhalation exposures to vapours should be included in the risk assessment a Tier 1 Screening calculation is peformed for a toddler. The risk from the inhalation of vapours of fludioxonil as considered to be negligible for the toddler (and by inference for infants, children and adults) if :

$0.328 \times (mwt \times VP) / AEL_{Long\text{-}term} < 1$.

Where: mwt – the molecular weight of the active substance and VP is its vapour pressure

Hence, taking into account a molecular weight of 248.2 g/mol, a vapour pressure of 3.9×10^{-7} Pa at room temperature and a $AEL_{Long\text{-}term}$ of 0.37 mg/kg bw/day, , the risk to a toddler is determined as: $0.328 \times (248.8 \times 3.9 \times 10^{-7})/0.37 = 8.58 \times 10^{-5.}$

Thus the inhalation exposure to residues of fludioxonil indoors can be considered to be neglibile and excluded from the risk assessment for adults, infants, todders and children.

Summary table: systemic secondary exposure of the general public					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake[1]**	**Estimated dermal uptake (mg fludioxonil/kg bw/day)**	**Estimated oral uptake (mg fludioxonil/kg bw/day)**	**Estimated total uptake (mg fludioxonil/kg bw/day)**
Scenario [PT7-13] **Toddler – touching wet painted surface**	Not relevant	Not relevant	1.3×10^{-3}	Not relevant	1.3×10^{-3}
Scenario [PT7-14] **Toddler – touching wet painted surface and mouthing**	Not relevant	Not relevant	1.3×10^{-3}	4.3×10^{-3}	5.6×10^{-3}
Scenario [PT7-15] **Toddler – touching dry painted surface**	Not relevant	Not relevant	5.6×10^{-5}	Not relevant	5.6×10^{-5}
Scenario [PT7-16] **Toddler – touching dry painted surface and mouthing**	Not relevant	Not relevant	5.6×10^{-5}	9.4×10^{-4}	1.0×10^{-3}

Scenario [PT7-17] **Adult – laundry of contaminated coveralls after paint spraying activities**	Not relevant	Not relevant	7.6×10^{-4}	Not relevant	7.6×10^{-4}
Scenario [PT7-18] **Toddler – dermal contact with wet preserved materials (e.g. mineral sealants and grouts)**	Not relevant	Not relevant	2.2×10^{-4}	Not relevant	2.2×10^{-4}
Scenario [PT7-19] **Toddler – dermal contact with wet preserved materials and mouthing**	Not relevant	Not relevant	2.2×10^{-4}	7.2×10^{-4}	9.4×10^{-4}
Scenario **Long term inhalation exposure for volatilised residues**	Not relevant	8.6×10^{-5}	Not relevant	Not relevant	Not relevant

[1]Indirect inhalation exposures are not considered relevant.

PT-9 (preserved materials) and PT10 (preserved masonry)

No further calculations due to secondary, indirect exposures are envisaged for the uses of Sporgard WB in PT9 (use of preserved materials). No secondary, indirect exposures are envisaged for the uses of Sporgard WB in PT10.

8.6.2 Combined scenarios

Regarding combined exposure scenarios for members of the public arising from secondary, indirect exposures, relevent worst-case scenarios have been addressed in the previous section and no further combined scenarios are considered relevent. The potential for members of the public to come in direct contact with preserved products is low due their infrequenct use and any indirect exposure will be incidental. For example, a worst-case scenario would be considered to be a toddler who touches a wet painted surfaces (dermal exposure) and subsequently mouths a contamined hand. Such events would be considered to be rare and multiple contamination incidents unlikely, since children would be expected to be excluded from areas where painting or other DIY activities are being carried out.

Regarding secondary exposures in adults, while it is possible that a person who regularly washes out coveralls used by professionals may also used preserved products for example, when performing DIY tasks, the contribution on account of the secondary exposures is minor and not considered to be any worse that the combined exposures determined for non-professionals in section 2.7.9.

8.7 DIETARY EXPOSURE

Human exposure to fludioxonil through the diet resulting from its use in biocidal preparations is estimated to be insignificant; it is therefore not necessary to propose or justify acceptable residues.
Fludioxonil is not sprayed/applied on food and feedingstuffs and is unlikely to come into direct contact with food based on its use pattern.
Biocidal preparations of fludioxonil will not be used where food for human consumption is prepared, consumed or stored, or where animal foodstuff is prepared, consumed or stored. Additional studies relating to the behaviour of the residues of active substance, its degradation products, reaction products and metabolites in treated or contaminated foods or foodstuffs are therefore not necessary.
Setting MRLs in food and feedstuffs is not necessary.

Fludioxonil is listed on Annex I of Directive 91/414/EEC
Fludioxonil has an ADI of 0.37 mg/kg bw/d.
According to the Directive 91/414/EEC review of fludioxonil, none of the identified animal, plant or environmental metabolites of fludioxonil was considered to be of toxicological relevance (EFSA conclusion, 2007).

8.8 EXPOSURE ASSOCIATED WITH PRODUCTION, FORMULATION AND DISPOSAL OF THE BIOCIDAL PRODUCT

Potential exposures during the manufacture of the active substance and its formulation into the biocidal product are considered under The Chemical Agents at Work Directive (98/24/EC, within 89/391/EEC) and are 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 protection12) whenever exposure to the active ingredient or other

[12] The Personal Protective Equipment as Work Regulations 1992 (EU Directive 89/656/EEC)

ingredients is likely. These regulations competently control for operator exposure to the biocides and substance of concern in the paint formulation.

9 ENVIRONMENTAL EXPOSURE ASSESSMENT

Fludioxonil is used as a fungicidal active substance in the material preservative product Sporgard WB. The product contains 2% (w/w) fludioxonil in combination with the active substances azoxystrobin and thiabendazole. The other two a.s. are not the subject of this dossier and will be treated as "substances of concern". The product is used to prevent microbial spoilage of materials, primarily paints, sealants and coatings (PT7), industrial paper used in the manufacturing of drywall/gypsum wallboards (PT9) and the preservation of the gypsum central core in drywall boards (PT10).

Intended uses and concentrations of fludioxonil

Biocidal product	Field of use envisaged	Concentration of product in end-use material	Concentration of fludioxonil in end-use material
PT7 Film preservative			
Sporgard WB Fludioxonil 2% w/w content	Paints and coatings (aqueous emulsions) Indoor use	0.15-1.6% w/w	0.003-0.032% w/w
	Mineral sealants and fillers (e.g. grout, mortar) Indoor use	0.08-1.6% w/w	0.002-0.032% w/w
PT9.02 – Paper preservative			
Sporgard WB Fludioxonil 2% w/w content	Paper (drywall lining) Indoor use	0.25-0.5% w/w (dry paper)	0.005-0.010% w/w
PT10 Masonry preservative			
Sporgard WB Fludioxonil 2% w/w content	Drywall gypsum powder Indoor use	0.05-1.6% w/w	0.001-0.032% w/w

9.1 EMISSION ESTIMATION

For the assessment of the environmental exposure of the biocidal product (b.p.) the following life cycle stages are selected to be relevant:

- Production of a.s. (cover PT7, 9 and 10)
- Formulation of b.p. (cover PT7, 9 and 10)
- Formulation of end-use product (diffent procedure for PT7, 9 and 10)
- Application by brush & roller (only relevant for PT7)
- Service life (only relevant for PT7)

The disposal step is not taken into consideration because emissions are assumed to be of minor relevance compared to releases due to in-situ application and use. Furthermore, the ESD for film preservatives (EC DG ENV and RIVM; 2004) states that, in case of landfill, it is very unlikely that the total remaining amount of a.s. in the paints will be released. Additionally, in several countries schemes

for controlled treatment of excess/waste are in place. In case of incineration, organic substances will be destroyed and no emissions are expected.

9.1.1 Release estimation for production of a.s. (cover PT7, 9 and 10)

The active substance is manufactured outside the EU (imported as a solid). Therefore no exposure data with respect to the production step are required.

9.1.2 Release estimation for formulation of b.p. (cover PT7, 9 and 10)

Currently, the biocidal product Sporgard WB is manufactured outside the EU. It cannot be excluded that in future the biocidal product might be (partially) produced in EU provided authorisation of the active is granted. In this case, the active substance fludioxonil (powder) will be delivered in PE containers. Dosing of the active substance is performed automatically into a vessel containing the other co-formulants. Fludioxonil is mixed into the liquid formulation by stirring. The biocidal product Sporgard WB is an aqueous dispersion. The product is pumped automatically from the mixing vessel into 1000 L IBC or into 200 L drums with HDPE inliner. No waste is released into the environment from the industrial process as the formulation process is highly automated.

9.1.3 Release estimation from manufacture of end-use product (cover PT7, 9 and 10)

All uses of fludioxonil as a material preservative involve incorporation of the biocidal product into the matrix of the end-use material. The process of incorporation is conducted industrially by means of an automated dosing system handled by professional workers and releases to the environment are controlled by industrial regulations and are expected to be negligible. Nevertheless, exposure concentrations are calculated for the manufacturing of the different end-use products, i.e. PT7, 9 and 10, where the biocidal product is applied. A tonnage based approach is applied for this. Find calculations in the *confidential* Appendix III.

9.1.4 Release estimation from application (cover PT7, 9 and 10)

Materials treated with fludioxonil are used in indoor applications where direct release to the environment can safely be excluded. However, environmental exposure may occur via secondary routes following, for example, disposal of washing water to drain and release through sewage treatment plant (STP). The use of fludioxonil treated materials can be either by professional (industrial) workers performing daily work tasks or consumers (private) conducting occasional DIY tasks. For the use in PT7, the scenario in the ESD for PT7 (emission from decorative paints) for private use is used as a worst case compared to the one for professional use. This emission estimation is a tonnage bases approach and is therefore provided in the *confidential* Appendix III. For the use in PT9 and PT10, it is assumed that there will be no emission to any environmental compartment during installation and during the following service life of the drywall/gypsum wallboards. When installing the wallboards, these might be cut to fit the place where they are placed, waste from this will be solid waste and will be handled according to national regulation. During the following use phase the wallboards are covered by wallpaper/paint and when removing the wallboards at the waste stage these are handled as solid waste and are handled according to national regulation. Therefore calculations are only performed for PT7.

General information

Assessed PT	PT 7: Paints, mineral sealants and silicon coatings – indoor use PT 9: Paper for the manufacturing of drywall/gypsum wallboards – indoor use PT 10: Gypsum central core in drywall boards – indoor use Sporgard WB is used industrially by professional workers in the preparation of treated materials (PT 7, 9 and 10). The end-use treated materials may be used by professionals and non-professionals depending on the particular item.
Assessed scenarios	PT7: Scenario 1: Release estimation from industrial use of biocidal product (tonnage approach) Scenario 2a: Release estimation from application and service life from decorative paint (tonnage approach) Scenario 2b: Release estimation from application and service life from sealants (consumption approach) PT9: Scenario 3: Release estimation from manufacture of paper used on drywall/gypsum wallboards (consumption approach) Scenario 4: Release estimation from industrial use of biocidal product (tonnage approach) PT10: Scenario 5: Release estimation industrial use of biocidal product (tonnage approach)
ESD(s) used	PT7: Emission Scenario Document for Product Type 7: Environmental Emission Scenarios for Biocides used as Film Preservatives, January 2004 City scenario: Leaching from paints, plasters and fillers applied in urban areas (NL, 2015) PT9: Emission scenario document for biocides used in paper coating and finishing (PT 6, 7 and 9), May 2001 Volume IV, Part B, Appendix 7 – Tonnage based approach – Emission factors for different use categories (A/B – Tables), April 2015
Approach	PT7: Scenario 1: Tonnage based approach (Industrial use of biocidal product) Scenario 2a: Tonnage based approach (application and service life of end-use product) Scenario 2b: Consumption based approach (application and service life of end-use product) PT9: Scenario 3: Consumption based approach (manufacture of end-use product) Scenario 4: Tonnage based approach (Industrial use of biocidal

	product) PT10: Scenario 5: Tonnage based approach (Industrial use of biocidal product)
Distribution in the environment	Calculated based on guidance on the BPR: Volume IV Environment, Part B Risk Assessment (active substance) (Vol. IV, Part B, 2015). Volume IV, Part B, Appendix 7 – Tonnage based approach – Emission factors for different use categories (A/B – Tables), April 2015
Groundwater simulation	Groundwater concentrations for soil photodegradation products were calculated using FOCUS PEARL 4.4.4 (find calculations in the end of the *confidential* appendix)
Confidential Annexes	YES: In the *confidential* Appendix III the tonnage based scenarios 1, 2a, 4 and 5 are provided
Remarks	Tonnage data for the calculation of the release estimation are provided in IUCLID

Biocidal product specific data

No product specific data are available that may influence the fate, distribution or the toxicity of fludioxonil.

Scenario 1 (PT7)

For PT7 (paints, mineral sealants and silicon coatings) a scenario is included for the industrial use of the biocidal product for production of the end-product, calculations are performed based on IC 14 (paints, lacquers and varnishes industry) from the A/B tables (Vol IV, Part B, Appendix 7, 15/4-15). This emission is considered as a point source from the industry that is formulating the end-use product. Find input values below.

Parameters for calculating the local emission			
Input	**Value**	**Unit**	**Remarks**
Scenario 1: Industrial use of the biocidal product			
Annual tonnage in the EU (PT7) of the active substance	*Confidential*	ton/year	S (Information from the applicant, IUCLID 7.5)
Annual tonnage in the EU of the biocidal product	*Confidential*	ton/year	Concentration of fludioxonil in the biocidal product is 2%
Fregion	0.1	-	D (TGD, 2003)
Fmainsource	0.3	-	D (Table B3.13, A/B-tables)
Fwastewater	0.005	-	D (Table A3.15, A/B-tables)
Temission	*Confidential*	days	D (Table B3.13, A/B-tables), No of days is derived from 3.333*f*T = 2*3.333*T (Vol IV, Part B, 15/4-15)

Output			
Local emission of active substance to waste water	*Confidential*	kg/d	During emission episode

S: Set value; D: Default value

Scenario 2a (PT7)
For PT7 (paints, mineral sealants and silicon coatings) a scenario is included for the use and service life indoor of the end-use product, calculations are performed based on ESD PT7 (January 2004). This emission is considered as a wide dispersive use from households in a catchment area. Find input values below.

Parameters for calculating the local emission			
Input	**Value**	**Unit**	**Remarks**
Scenario 2a: Application and service life of the end-use product			
Annual tonnage in the EU (PT7)	*Confidential*	ton/year	S (Information from the applicant, IUCLID 7.5)
Fregion	0.1	-	D (Table 4.1 in ESD PT7)
Fmainsource	0.002	-	
Fwastewater (private use)	0.03	-	
		-	
Fdisposal	0.95	-	
Temission	150	days	
Output			
Local emission of active substance to waste water	*Confidential*	kg/d	During emission episode

S: Set value; D: Default value

Scenario 2b (PT7)
For PT7 (paints, mineral sealants and silicon coatings) a scenario is included for the use and service life indoor of the end-use product in wet cleaning areas for use in sealants. The calculation is based on the city scenario (NL, 2015). According to the city scenario a total surface area of 0.12 m2 per house is used for sealants in bathrooms.

The end-product is used either by amateurs or by professional craftsmen. With regard to the assessment, any significant difference between professional and non-professional application were ignored, as both professionals and non-professionals are expected to use the same amount and further no loss during application will be expected for both groups of users. The end-product is a ready to use product, thus a pre-treatment is not included in the risk assessment. The final concentration in the end-product is maximum 0.032% (w/w) fludioxonil.

In the emission calculation, only the release during service life will be assessed, since losses during application can be excluded because no spray drift, dripping or rinsing occurs.
When the silicone sealant gets in contact with water during the service life a slight release of fludioxonil into the water phase can be expected.

Taking into account that the product will be used as a single-application procedure with a service life of 10 years (according to the city scenario), it is assumed that the whole incorporated fludioxonil (100%)

will be leached in equal parts within the service life period, see Table 1. As the product is designed to adhere to joints and will not be washed off quickly only a long-term assessment (10 years) will be performed and not a short term assessment (30 days), this procedure follows the guidance given in the city scenario (NL, 2015).

Parameters for calculating the local emission			
Input	**Value**	**Unit**	**Remarks**
Scenario 2b: Service life of the end-use product			
Amount of a.i. in the corresponding silicone sealant	0.032	%(w/w)	Information provided by the applicant
Total amount of sealant	5.88	kg/m^2	City scenario (NL, 2015)
Leachable area of house	0.12	m^2	City scenario (NL, 2015)
Number of houses draining to one STP	4000	-	Vol IV, Part B (2013)
Duration of assessment period	3650	days	City scenario (NL, 2015)
Output			
Local emission of active substance to waste water	2.47×10^{-4}	kg/d	During emission episode

The local emission to a STP from 4,000 households was calculated to be 2.47×10^{-4}.

Scenario 3 (PT9)

The described use of Sporgard WB is coating of previously manufactured paper rather than use at the paper mill, it is expected that this process is performed at the same time as paper is applied to gypsum plates. According to the ESD for biocides used in paper coating and finishing (PT6, 7 and 9) emissions from off-line coating are expected to be negligible, furthermore the applicant confirms that the coating takes place in closed systems, therefore no exposure calculations will be performed for this process.

Scenario 4 (PT9)

For PT9 (paper used on drywall/gypsum wallboards) a scenario is included for the industrial use of the biocidal product for the preparation of the end-use product, calculations are performed based on IC 12 (pulp, paper and board industry) UC ≠ 10 & 45, from the A/B tables (Vol IV, Part B, 15/4-15). This emission is considered as a point source from the industry where the industrial use is applied.

Find input values below.

Parameters for calculating the local emission			
Input	**Value**	**Unit**	**Remarks**
Scenario 4: Industrial use of the biocidal product			
Annual tonnage in the EU (PT9)	*Confidential*	ton/year	S (Information from the applicant, IUCLID 7.5)
Annual tonnage in the EU of the biocidal product	*Confidential*	ton/year	Concentration of fludioxonil in the biocidal product is 2%
Fregion	0.1	-	D (TGD, 2003)
Fmainsource	0.333 or	-	D (Table B3.10, A/B-tables), tonnage is biocidal product,

	0.05		highest value is used
Fwastewater (private use)	0.0001	-	D (Table A3.12 for printing and allied processes, MC=2, defaults, A/B-tables)
Temission	*Confidential*	days	D (Table B3.10, A/B-tables), No of days is derived from 2f*T = 2*0.333*T (Vol IV, Part B, 15/4-15)
Output			
Local emission of active substance to waste water	*Confidential*	kg/d	During emission episode

S: Set value; D: Default value

Scenario 5 (PT10)

For PT10 (gypsum central core in drywall boards) a scenario is included for the industrial use of the biocidal product for production of the end-use product, calculations are performed based on IC 12 (pulp, paper and board industry) UC ≠ 10 & 45, from the A/B tables (Vol IV, Part B, 15/4-15). This emission is considered as a point source from the industry.
Find input values below.

Parameters for calculating the local emission			
Input	**Value**	**Unit**	**Remarks**
Scenario 5: Industrial use of the biocidal product			
Annual tonnage in the EU (PT10)	*Confidential*	ton/year	S (Information from the applicant, IUCLID 7.5)
Annual tonnage in the EU of the biocidal product	*Confidential*	ton/year	Concentration of fludioxonil in the biocidal product is 2%
Fregion	0.1	-	D (TGD, 2003)
Fmainsource	0.333 or 0.05	-	D (Table B3.10, A/B-tables), tonnage is biocidal product, highest value is used
Fwastewater (private use)	0.0001	-	D (Table A3.12 for printing and allied processes, MC=2, defaults, A/B-tables)
Temission	*Confidential*	days	D (Table B3.10, A/B-tables), No of days is derived from 2f*T = 2*0.333*T (Vol IV, Part B, 15/4-15)
Output			
Local emission of active substance to waste water	*Confidential*	kg/d	During emission episode

S: Set value; D: Default value

Calculations for all scenarios

The local emission to the sewage treatment plant from each scenario is shown in the following table.

Resulting local emission to relevant environmental compartments			
PT and stage	**Compartment**	**Local emission during emission episode ($Elocal_{compartment}$) [kg/d]**	**Remarks**
PT7			
Industrial use of biocidal product	STP (Scenario 1)	*Confidential*	Point source
Private use and service life of end-use product (paint)	STP (Scenario 2a)	*Confidential*	Wide dispersive use
Private use and service life of end-use product (sealant)	STP (Scenario 2b)	2.47×10^{-4}	Wide dispersive use
PT9			
Industrial use of biocidal product	STP (Scenario 3)	0.000	Point source
Industrial use of biocidal product	STP (Scenario 4)	*Confidential*	Point source
Private use and service life of end-use product	No emissions to any compartment	0.000	Wide dispersive use
PT10			
Industrial use of biocidal product	STP (Scenario 5)	*Confidential*	Point source
Private use and service life of end-use product	No emissions to any compartment	0.000	Wide dispersive use

9.2 FATE AND DISTRIBUTION IN EXPOSED ENVIRONMENTAL COMPARTMENTS

In the following table relevant receiving compartments are identified.

Identification of relevant receiving compartments based on the exposure pathway									
	Fresh-water	**Sediment**	**Sea-water**	**Seawater sediment**	**STP**	**Air**	**Soil**	**Ground-water**	**Other**
PT7									
Industrial use *Scenario 1*	+	+	-	-	++	+	+	+	-

Private use and service life *Scenario 2a and 2b*	+	+	-	-	++	+	+	+	-
PT9									
Industrial use *Scenario 4*	+	+	-	-	++	+	+	+	-
Private use and service life *No emission*	-	-	-	-	-	-	-	-	-
PT10									
Industrial use *Scenario 5*	+	+	-	-	++	+	+	+	-
Private use and service life *No emission*	-	-	-	-	-	-	-	-	-

++: direct emission
+: indirect emission
-: no emission

For the calculation of predicted environmental concentrations of fludioxonil in relevant compartments the input parameters in the following table are used.

Input parameters (only set values) for calculating the fate and distribution in the environment			
Input	**Value**	**Unit**	**Remarks**
Molecular weight	248.2	g/mol	
Melting point	199.8	°C	
Boiling point	306	°C	Decomposes at 306 °C before boiling
Vapour pressure (at 25 °C)	3.9×10^{-7}	Pa	Extrapolated
Water solubility (at 25 °C)	1.8	mg/L	Cover pH 5 to 9
Log10 Octanol/water partition coefficient	4.12	---	Experimental flask method
Organic carbon/water partition coefficient ($K_a$oc)	145,600	L/kg	Arithmetic mean, n=5
Henry's Law Constant (at 20 °C)	2.57×10^{-5}	$Pa/m^3/mol$	Calculated

Biodegradability	Not biodegradable		Tested in a CO_2 evolution test
Rate constant for STP	No data	h^{-1}	
DT_{50} for biodegradation in surface water	1326	d (at 12ºC)	Only data from the whole system of a water/sediment degradation test is available
DT_{50} for hydrolysis in surface water	stable	d (at 12ºC /pH5, 7 and 9)	No degradation was found in the test
DT_{50} for photolysis in surface water	28	d (at 12ºC)	Highest value of two endpoints
DT_{50} for degradation in soil	502	d (at 12ºC)	Geometric mean from 8 soils
DT_{50} for degradation in air	6.7	hr (24 hour day)	Estimated value from AOPWIN
DT_{50} for degradation in sediment	no data	d or hr	Only data from the whole system of a water/sediment degradation test is available

The calculated distribution of fludioxonil in the sewage treatment plant can be found in the following table based on calculations with EUSES 2.1.2.

Calculated fate and distribution in the STP		
Compartment	**Percentage [%]**	**Remarks**
	Scenario 1 to 4	
Air	2.45×10^{-6}	Calculated with EUSES 2.1.2
Water	12.4	
Sludge	87.6	
Degraded in STP	0	

9.3 CALCULATED PEC VALUES

Fludioxonil

In the Table below PEC values are calculated for fludioxonil for the relevant scenarios.

Summary table on calculated PEC values for fludioxonil							
	PEC_{STP} [a]	**PEC_{water}** [a]	**PEC_{sed}** [a]	**$PEC_{soil30d}$** [b]	**$PEC_{soil180d}$** [b] Agr. soil	**PEC_{GW}** [b] Agr. soil	**PEC_{air}** [b]
	[mg/L]	[mg/L]	[mg/kg_{wwt}]	[mg/kg_{wwt}]	[mg/kg_{wwt}]	[µg/l]	[mg/m^3]
PT7							
Industrial use *Scenario 1*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2a*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2b*	1.53×10^{-5}	1.26×10^{-6}	3.98×10^{-3}	1.10×10^{-3}	9.98×10^{-4}	4.31×10^{-4}	1.69×10^{-15}
PT9							
Industrial form. *Scenario 3*	0	0	0	0	0	0	0
Industrial use *Scenario 4*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0	0
PT10							
Industrial use *Scenario 5*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life	0	0	0	0	0	0	0

Summary table on calculated PEC values for fludioxonil							
	PEC_{STP} [a]	**PEC_{water}** [a]	**PEC_{sed}** [a]	**$PEC_{soil30d}$** [b]	**$PEC_{soil180d}$** [b] Agr. soil	**PEC_{GW}** [b] Agr. soil	**PEC_{air}** [b]
	[mg/L]	[mg/L]	[mg/kg_{wwt}]	[mg/kg_{wwt}]	[mg/kg_{wwt}]	[µg/l]	[mg/m^3]
No emission							
[a] Predicted environmental concentrations are calculated for the emission episode [b] Predicted environmental concentrations are calculated for the annual average							

Degradation products in water

The major photo-degradation products (>10% applied fludioxonil) in the water phase are identified as CGA 339833 (max. 30.5%), CGA 344623 (max. 12.4%) and A5 (max 11.5%). In the Table below PEC values are calculated for these photo-degradation products in the water and sediment phase. Concentrations in the water phase are calculated based on the concentration of fludioxonil in the water phase times the difference in molar weight and times the formation rate given above. For CGA 339833: 1.26 x 30.5 = 38.4% is formed, for CGA 344623: 1.20 x 12.4 = 14.9% is formed and for A5: 1.02 x 11.5 = 11.8% is formed. Values in sediment are calculated using the Ksusp-water of the degradation products: 1.15 m^3/m^3 (CGA 339833), 1.16 m^3/m^3 (CGA 344623) and 1.45 m^3/m^3 (A5).

Summary table on calculated water and sediment PEC values for CGA 339833, CGA 344623 and A5						
	PEC_{water} [a]	**PEC_{sed}** [a]	**PEC_{water}** [a]	**PEC_{sed}** [a]	**PEC_{water}** [a]	**PEC_{sed}** [a]
	[mg/L]	[mg/kg_{wwt}]	[mg/L]	[mg/kg_{wwt}]	[mg/L]	[mg/kg_{wwt}]
	CGA 339833		**CGA 344623**		**A5**	
PT7						
Industrial use *Scenario 1*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2a*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2b*	4.83×10^{-7}	4.83×10^{-7}	1.88×10^{-7}	1.89×10^{-7}	1.49×10^{-7}	1.88×10^{-7}

Summary table on calculated water and sediment PEC values for CGA 339833, CGA 344623 and A5						
	PEC_{water} [a]	**PEC_{sed} [a]**	**PEC_{water} [a]**	**PEC_{sed} [a]**	**PEC_{water} [a]**	**PEC_{sed} [a]**
	[mg/L]	[mg/kg_{wwt}]	[mg/L]	[mg/kg_{wwt}]	[mg/L]	[mg/kg_{wwt}]
	CGA 339833		**CGA 344623**		**A5**	
PT9						
Industrial form. *Scenario 3*	0	0	0	0	0	0
Industrial use *Scenario 4*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0
PT10						
Industrial use *Scenario 5*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0
[a] Predicted environmental concentrations are calculated for the emission episode						

Degradation products in soil

The major photo-degradation products (>10% applied fludioxonil) in the soil phase are identified as CGA 339833 (max. 9.1%), CGA 192155 (max. 11.7%) and CGA 265378 (max 12.3%). In the Table below PEC values are calculated for these photo-degradation products in the soil and groundwater phase. Concentrations in the soil phase are calculated based on the concentration of fludioxonil in the soil phase times the difference in molar weight and times the formation rate given above. For CGA 339833: 1.26 x 9.1 = 11.45% is formed, for CGA 192155: 0.81x 11.7 = 9.53% is formed and for CGA 265378: 1.12x 12.3 = 13.79% is formed. Values in groundwater are calculated using the Ksoil-water of the degradation products: 0.500 m^3/m^3 (CGA 339833), 0.502 m^3/m^3 (CGA 192155) and 1.01 m^3/m^3 (CGA 265378).

Summary table on calculated water and sediment PEC values for CGA 339833, CGA 192155 and CGA 265378

	$PEC_{soil30d}$ [b]	**PEC_{GW}** [b] Agr. soil	**$PEC_{soil30d}$** [b]	**PEC_{GW}** [b] Agr. soil	**$PEC_{soil30d}$** [b]	**PEC_{GW}** [b] Agr. soil
	[mg/kg_{wwt}]	[µg/l]	[mg/L]	[mg/kg_{wwt}]	[mg/L]	[mg/kg_{wwt}]
	CGA 339833		**CGA 192155**		**CGA 265378**	
PT7						
Industrial use *Scenario 1*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2a*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *Scenario 2b*	1.26×10^{-4}	0.43	1.05×10^{-4}	0.36	1.52×10^{-4}	0.26
PT9						
Industrial form. *Scenario 3*	0	0	0	0	0	0
Industrial use *Scenario 4*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0
PT10						
Industrial use *Scenario 5*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*	*Confidential*
Private use and service life *No emission*	0	0	0	0	0	0
[b] Predicted environmental concentrations are calculated for the annual average						

As a number of the soil photodegradation products were calculated to be greater than the regulatory limit of 0.1 µg/L in groundwater, further modelling was conducted using the groundwater model FOCUS PEARL 4.4.4. An application rate for soil was calculated from the aggregated soil concentration for each metabolite based on the knowledge that EUSES had calculated soil PECs assuming a mixing depth of 0.2 m and soil density of 1700 kg/m^3. Aggregated soil concentrations for CGA339833, CGA192155 and CGA265378 were x, y and z mg/kg wwt respectively (find values in the *confidential* appendix). The application rates for FOCUS modelling for CGA 339833, CGA 192155 and CGA265378 were calculated to be x, y and z kg/ha respectively (find values in the *confidential* appendix). The Koc values for modelling were calculated by QSAR. The soil degradation values used were the values presented in the EFSA conclusion for fludioxonil, which have been normalised to pF2 conditions and as such are suitable for use in FOCUS modelling. Application was considered to occur once per year on the 1st Jan, which is considered to be sufficiently representative for modelling purposes here. All FOCUS groundwater scenarios were included. Full inputs are presented in the table below. It should be noted that in ECHA's Guidance on the Biocidal Products Regulation, Volume IV Environment – Part B Risk Assessment (active substances) v1.0, it states that for substance approval only one of the nine scenarios needs to meet the required criteria according to BPR Annex VI, point 68. As such, only the lowest calculated scenarios were used for comparison to the regulatory threshold value of 0.1 µg/L.

Summary of FOCUS PEARL inputs for soil degradation prodcucts CGA 339833, CGA 192155 and CGA 265378		
Parameter	**Value**	**Comments**
CGA339833		
Molecular mass	312.19	-
Aqueous solubility (mg/L, 25ºC)	31000	Measured value
Vapour pressure (Pa, 25 ºC)	4.3×10^{-6}	Measured value
K_{OC} (mL/g)	10	QSAR estimate
K_{OM} (mL/g)	5.8	From K_{FOC}/1.724
Freundlich exponent	0.9	Default value
DT_{50} (d, 20°C/pF2)	8.7	Mean at 20°C and pF2 (from EFSA conclusion for fludioxonil)
Plant uptake factor	0	Worst case
CGA192155		
Molecular mass	202.12	-
Aqueous solubility (mg/L, 25ºC)	22000	Measured value
Vapour pressure (Pa, 25 ºC)	3.7×10^{-5}	Measured value
K_{OC} (mL/g)	10.07	QSAR estimate
K_{OM} (mL/g)	5.84	From K_{FOC}/1.724
Freundlich exponent:	0.9	Default value
DT_{50} (d, 20°C/pF2)	12.9	Mean at 20°C and pF2 (from EFSA conclusion for fludioxonil)
Plant uptake factor	0	Worst case
CGA265378		
Molecular mass	278.17	-
Aqueous solubility (mg/L, 25ºC)	120	Measured value
Vapour pressure (Pa, 25 ºC)	8.4×10^{-8}	Measured value
K_{OC} (mL/g)	27	Arithmetic mean from LoEP (n=7)
K_{OM} (mL/g)	15.71	From K_{FOC}/1.724
Freundlich exponent:	0.9	Default value
DT_{50} (d, 20°C/pF2)	19	Worst-case non-normalised value (from EFSA conclusion for fludioxonil)
Plant uptake factor	0	Worst case

The PECs calculated for groundwater are presented in the table below.

Summary of FOCUS PEARL calculated groundwater PECs for CGA339833, CGA192155 and CGA265378			
Scenario	80th percentile PECgw (µg/L)		
	CGA339833	CGA192155	CGA265378
	PEARL	PEARL	PEARL
Châteaudun	*Confidential*	*Confidential*	*Confidential*
Hamburg	*Confidential*	*Confidential*	*Confidential*
Jokioinen	*Confidential*	*Confidential*	*Confidential*
Kremsmünster	*Confidential*	*Confidential*	*Confidential*
Okehampton	*Confidential*	*Confidential*	*Confidential*
Piacenza	*Confidential*	*Confidential*	*Confidential*
Porto	*Confidential*	*Confidential*	*Confidential*
Sevilla	*Confidential*	*Confidential*	*Confidential*
Thiva	*Confidential*	*Confidential*	*Confidential*

9.4 PRIMARY AND SECONDARY POISONING

Primary poisoning

No primary poisoning is foreseen for the product.

Secondary poisoning

According to current guidance (REACH R16, point R16.6.7, a detailed assessment of secondary poisoning is required if a substance has a bioaccumulation potential, **and** is neither readily biodegradable nor hydrolysable, **and** may also cause toxic effects if accumulated in higher organisms.

The assessment of the secondary poisoning route should first consider the indications for bioaccumulation potential.
Although the log Kow determined for fludioxonil is 4.12, a study of bioconcentration in *L. macrochirus* gave steady-state estimated BCF values of 56 to 58, 741 to 749 and 365 to 366 L/kg ww in edible portions, non-edible portions and whole fish, respectively. Fludioxonil residues were rapidly eliminated following the termination of exposure, with DT_{90} values of < 2 days for residues in whole fish. Fludioxonil therefore exhibits only limited bioconcentration behaviour in fish, with rapid depuration characteristics. A BCF value of 159 L/kg ww has been calculated for earthworms. The observed and predicted BCF values are all lower than the trigger value of 2000 and fludioxonil therefore does not qualify for classification as bioaccumulative (B) or very bioaccumulative (vB).

The potential for accumulated residues to cause toxic effects in higher organisms should be considered next, with reference to the classification categories Very Toxic (T+), Toxic (T) or harmful (Xn), accompanied by at least one of the risk phrases R48, R60, R61, R62, R63 or R64, or indications of endocrine disruption.
Fludioxonil does not trigger classification as T+, T or Xn and none of the relevant risk phrases apply. The active substance has not been identified as having endocrine disrupting properties *in vivo*. Although these aspects form part of the conservative risk assessment approach for humans, current guidance considers that they will also be protective of other non-target top predator organisms in the environment.

On this basis, consideration of the secondary poisoning exposure route is not relevant for fludioxonil.

10 ASSESSMENT OF EFFECTS ON HUMAN HEALTH FOR THE PRODUCT

10.1 PRODUCT(S)

The acute toxicity studies were conducted in 2007. In the meantime minor adjustments in the active substance content of the composition of the end use products Sporgard WB (thiabendazole/azoxystrobin/fludioxonil SC) were done, there was no change in co-formulants. Due to the fact that there are only minor deviations between the composition of the formulation Sporgard WB used in the below mentioned studies (19.2% TBZ, 19.6% AZ, 1.96% FDL) and the current composition of the product Sporgard WB as stated in section 2.3 (19.1% TBZ, 19.8% AZ, 1.96% FDL), it is considered that the available toxicity data are adequate. The minor change in concentration of Thiabendazole and Azoxystrobin in the formulation Sporgard WB will not have an impact on the classification of the product. Therefore, new toxicological studies are not justified.
Sporgard WB is an aqueous dispersion and the type of formulation can be described as a suspension concentrate (SC).

Overall Sporgard WB was shown, in a battery of acute toxicity tests, not to be toxic to human health and not to require any classification for human health hazards. The product contains one active substance, azoxystrobin, which is at the moment regarded as a substance of concern (since it is not included in annex I or have a draft CAR with reference values in another PT). However the current harmonized classification of the substance does not give rise to concern or classification of the product for long term effects, the acute effects are covered by studies on the product. No other substances/inert ingredients in the product are considered to be substances of concern according to the current definition of SOC. The product should however be labelled with EUH208: Contains BIT. May produce an allergic reaction.

10.2 DERMAL ABSORPTION

Please refer to the dermal absorption section under 3.1 Toxicokinetics in part A.

10.3 ACUTE TOXICITY

Summary of acute toxicity studies performed with the product							
Route	**Method Guideline GLP status, Reliability**	**Species/Strain/Sex No/group**	**Test substance, Dose levels (mg/kg bw)**	**Signs of toxicity (nature, onset, duration, severity, reversibility)**	**Value LD_{50}/LC_{50}**	**Remarks** *(e.g. major deviations)*	**Reference**
Acute orale	OECD 425 (up-and-down procedure) GLP 1	Sprague Dawley (SD) rat Limit test: 1 animal Main test: 9 animals in total (1 to 4 animals/dose)	Sporgard WB ([redacted]) 175, 550, 1750 & 5000	1750 mg/kg bw: All rats displayed hypoactivity, piloerection and/or diarrhea following dosing. Recovered by day 1. 5000 mg/kg bw: toxic signs noted prior to death included hypoactivity, hunched posture, piloerection, ano-genital staining, diarrhea and/or soft feces	5000 mg/kg bw	-	[redacted]. 2007d. (IUCLID 8.5.1-01)
Acute dermale	OECD 402 GLP 1	SD rat 5/sex	Sporgard WB ([redacted]) Semi-occlusion 5000 (limit test)	No clinical signs Dermal irritation (erythema) in 1 female on day 1	> 5000 mg/kg bw	-	[redacted] 2007f, (IUCLID 8.5.3-01)

Acute inhalation (nose-only)	OECD 403 GLP 1	SD rat 5/sex	Sporgard WB ([redacted])	2.59 mg/L ± 0.69	> 2.59 mg/L (maximum achievable concentration))	-	[redacted], 2007e, (IUCLID 8.5.2-01)

To investigated the **acute oral toxicity** Sporgard WB was administered by gavage to a group of female Sprague Dawley rats using the limit test at 5000 mg/kg bw followed by the Up and Down procedure (OECD 425) at levels of 175, 550, 1750 and 5000 mg/kg bw.
Animals appeared normal and gained weight throughout the study at 175 and 550 mg/kg bw. At 1750 mg/kg bw, all rats survived and gained weight during the study. All rats displayed clinical signs such as hypoactivity, piloerection and/or diarrhea following dosing but fully recovered by day 1. At 5000 mg/kg bw, toxic signs noted prior to death included hypoactivity, hunched posture, piloerection, ano-genital staining, diarrhea and/or soft feces. The only surviving rat appeared hypoactive and exhibited a reduced fecal volume, but recovered from these symptoms by Day 2 and appeared active and healthy for the remainder of the study and gained body weight over the 14-day observation period. In the pathological investigation no gross abnormality were observed. Discoloration of the intestines was reported in the 4 animals that died prior to study completion.
Acute oral LD_{50} of Sporgard WB in the female rat was found to be 5000 mg/kg bw (with a 95% profile-likelihood based confidence interval of 2016 mg/kg bw (lower) to 9810 mg/kg bw (upper) under the conditions of this study. Sporgard WB is not classified for acute oral toxicity in accordance with Regulation (EC) No 1272/2008.

In a **acute dermal** limit test 5000 mg/kg bw Sporgaard WB was applied for 24 hours under semi-occlusive conditions to the shorn dorsal skin of a group of Sprague-Dawley rats (5/sex). No deaths occurred during the study. No signs of toxicity were observed in any animals expect from one female showed erythema on Day 1 which recovered on Day 2. All animals survived and gained body weight thoughout the study. Gross necropsy did not reveal any treatment-related findings. The acute dermal LD_{50} of Sporgard WB in rats was found to be greater than 5000 mg/kg bw under the conditions of this study. Sporgard WB shall therefore not be classified for acute dermal toxicity in accordance with Regulation (EC) No 1272/2008.

In the **acute inhalation limit test** (OCED 403) Sprague Dawley rats (5/sex) were exposed (nose only) for four hours to atmospheres containing Sporgard WB aerosol at a measured concentration of 2.59 mg/l (MMAD 3.2 µm). 97.8-98% of the particles had a particles size < 9 µm and 83-86.6% < 5.8 µm. The tested concentration is the maximum technically achievable by the testing laboratory following several pre-test trials. The animals were observed for 14 days following exposure. No deaths occurred and no signs of toxicity were reported. All animals gained weight throughout the study. No gross abnormalities were noted for any of the animals when necropsied at the end of the study. The acute inhalation LC_{50} of Sporgard WB in the rat was found to be >2.59 mg/l under the conditions of this study. Therefore Sporgard WB shall not be classified for acute inhalation toxicity in accordance with Regulation (EC) No 1272/2008.

10.3.1 Overall conclusion on acute toxicity

Value used in the Risk Assessment – Acute toxicity	
Value(s)	Acute oral LD_{50}= 5000 mg/kg bw; acute dermal LD_{50}> 5000 mg/kg bw; acute inhalation LC50> 2.59 mg/L
Justification for the selected value	-
Classification for the product according to CLP and DSD	No classification warranted.

Fludioxonil was found to be of low toxicity via the oral, dermal and inhalation routes and is not classified according to Regulation (EC) No 1272/2008.

10.4 CORROSION AND IRRITATION

10.4.1 Skin corrosion and irritation

Summary table of animal studies on skin corrosion/irritation					
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance, Vehicle, Dose levels, Duration of exposure**	**Results (Draize scores mean 24-72h; all animals)**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 404 GLP 1	Rabbit, New Zealand albino 3 (males)	Sporgard WB ([redacted]) 0.5 mL	Erythema: 0.44 Odema: 0	Individual bodyweights were not recorded during the study.	[redacted] (2007a). (IUCLID 8.1-01)

The study was performed according to OECD 404. There were no signs of gross toxicity, adverse pharmacologic effects or abnormal behaviour. One hour after patch removal, very slight erythema and oedema were noted for all three treated sites. Individual animal Draize scores (mean 24-72h) for

erythema were 0.67, 0.33 and 0.33 with a mean for all animals of 0.44. The overall incidence and severity of irritation decreased with time. All animals recovered from irritation within 72 hours.

Sporgard WB shall not be classified for skin irritation in accordance with Regulation (EC) No 1272/2008.

10.4.2 Serious eye damage and eye irritation

Summary table of animal studies on serious eye damage and eye irritation					
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance Dose levels, Duration of exposure**	**Results** *Average score (24, 48, 72h) for all animals*	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 405 GLP 1	Rabbit, New Zealand albino 3 (males)	Sporgard WB ([redacted]) 0.1 mL (tested as supplied)	Cornea: 0 Iris: 0.33 Conjunctiva; Redness: 0.89 Conjunctiva; Chemosis: 0.33	-	[redacted] (2007b) (IUCLID 8.2-01)

The study was performed according to OECD 405. No corneal reactions were observed. Slight iritis and conjunctival chemosis was reported after 1 hour and persisted until 24 hours. The mean scores at 24-72 hours for iritis and conjunctival chemosis were below 1 and 2, respectively. The individual animal scores for iritis and chemosis were all 0.33 for all three rabbits. Conjunctival redness was observed in all animals at 1 hour and was reversible by 72 hours. The mean score at 24-72 hours for conjunctival redness was below 2 with individual animal's scores of 1, 0.67 and 1. Sporgard WB was mild eye irritant; findings were reversible by 72 hours. No classification is warranted for eye irritation in accordance with Regulation (EC) No 1272/2008 for Sporgard WB.

No human data is available.

10.4.3 Respiratory tract irritation

No animal or human data are available.

10.4.4 Overall conclusion on corrosion and irritation

Conclusion used in the Risk Assessment – Corrosion and irritation	
Value(s) or Conclusion(s)	Sporgard WB is not an eye or skin irritant.
Justification for the selected value/ conclusion	Negative OECD 404 and OECD 405 studies.
Classification of the product according to CLP and DSD	No classification warranted.

10.5 SENSITISATION

10.5.1 Skin sensitisation

Summary table of animal studies on skin sensitisation					
Method, Guideline, GLP status, Reliability	**Species, strain, sex, no/ group**	**Test substance, Vehicle, Dose levels, duration of exposure Route of exposure**	**Results** *(sensitised animals)*	**Remarks** *(e.g. major deviations)*	**Reference**
Buehler test (non-adjuvant) OECD 406 GLP 1	Guinea pig (m) Test group: 20 Naïve control group:10 Preliminary irritation group: 4	Sporgard WB ([redacted]) Topical induction once a week for three weeks Topical challenge (day 28) HNIC for challenge: 100%	0/20 Non-sensitising	-	[redacted] 2007c, (IUCLID 8.3-01)

The potential of Sporgard WB to induce delayed contact hypersensitivity (skin sensitisation) after topical application was investigated in a Buehler Test using guinea pigs (OECD 406). The undiluted test substance was topically applied to twenty guinea pigs, once each week for a three-week

induction period. Twenty-seven days after the first induction dose, a challenge dose of the test substance at its highest non-irritating concentration (HNIC, determined in the preliminary irritation screen to be 100%) was applied to a naive site on each guinea pig. A naive control group (ten animals) was maintained under the same environmental conditions and treated with the test substance at challenge only. Dermal reactions were reported 24 and 48 hours after challenge in tested animals, naïve control animals and positive control animals. Very faint erythema was noted for most test sites during the induction phase. Very faint to faint erythema was noted in 12 test sites at 24 hours and 7 test sites at 48 hours after challenge. Very faint erythema was also reported in the naïve control animals.The results of the historical positive control animals with alpha-Hexylcinnamaldehyde Technical (HCA) confirm the validity of the study.

Sporgard WB is not considered to be a skin sensitiser under the conditions of this study in accordance with Regulation (EC) No 1272/2008.

No human data is available.

10.5.2 Respiratory sensitisation

No animal or human data are available.

10.5.3 Overall conclusion on sensitisation

Sporgard WB is not considered to be a skin sensitiser under the conditions of this study in accordance with Regulation (EC) No 1272/2008.

Sporgard WB contains no active or non active components that are known respiratory sensitisers. Synergistic effects between components that would result in respiratory sensitisation are not suspeected. Overall classification of Sporgard WB as a respiratory senistiser is not required.

10.6 OTHER

No other data is available. Not required.

11 ENVIRONMENTAL EFFECTS ASSESSMENT FOR THE PRODUCT

The product Sporgard WB contains 2% (w/w) fludioxonil in combination with the active substances azoxystrobin and thiabendazole. The other two a.s. are not subject of this dossier and will be treated as "substances of concern".The two other active substances are not expected to affect the conclusions of the risk assessment for fludioxonil, therefore no further assessment is needed. The ecotoxicological properties of the product Sporgard WB may be derived from the properties of fludioxonil alone in this dossier as the two other active substances azoxystrobin and thiabendazole are evaluated in other CARs. Information on the ecotoxicity of fludioxonil is presented in Part A, Section 4.2. However further consideration of the additive toxicity of the three actives should be considered at the product authorisation stage when authorising the product Sporgard WB.

11.1 ATMOSPHERE

Information on the ecotoxicity of fludioxonil is presented in Part A, Section 4.2.

11.2 STP

Information on the ecotoxicity of fludioxonil is presented in Part A, Section 4.2.

11.3 AQUATIC COMPARTMENT

Information on the ecotoxicity of fludioxonil is presented in Part A, Section 4.2.

11.4 TERRESTRIAL COMPARTMENT

Information on the ecotoxicity of fludioxonil is presented in Part A, Section 4.2.

11.5 PRIMARY AND SECONDARY POISONING

Information on the ecotoxicity of fludioxonil is presented in Part A, Section 4.2.

Part C Risk characterisation of the biocidal product(s)

12 RISK CHARACTERISATION FOR HUMAN HEALTH

12.1 CRITICAL ENDPOINTS

12.1.1 Systemic effects

Study and duration	Route	Relevant effects	NOAEL (mg/kg bw day) Males/females Parental/ offspring/reproduction* Maternal/developmental**	LOAEL (mg/kg bw day) Males/females Parental/ offspring/reproduction* Maternal/developmental**	References
Rat (28 day)	Dermal	Phagocytic cells in the thymus in all females	1000/200	-/1000	[redacted] 1990 (IUCLID 8.9.1.3-01)
Rat (28 day)	Oral	Effects on bodyweight, clinical chemistry increased liver weights and hepatocyte hypertrophy; increased kidney weight and associated pathological changes including blood in urine.	100/100	1000/1000	[redacted]., 1990 (IUCLID 8.9.1.1-01)
Rat (90-day)	Oral	Effects in the kidney and liver at the two highest dose groups in both sexes (increased relative weights, chronic nephropathy, centrilobular hepatocyte hypertrophy)	64 / 70	428/462	[redacted].1990 (IUCLID 8.9.1.1-02)

Study and duration	Route	Relevant effects	NOAEL (mg/kg bw day) Males/females Parental/ offspring/reproduction* Maternal/developmental**	LOAEL (mg/kg bw day) Males/females Parental/ offspring/reproduction* Maternal/developmental**	References
Dog (90-day – with 28 day recovery)	Oral	Decreased body weight in high-dose animals, increased relative liver weight and histopathological changes in high-dose animals, signs of mild anaemia in high-dose females.	60 / 58.5	299/351	[redacted]., 1990 (IUCLID 8.9.1.1-03)
Dog (1-year)	Oral	Reduced body weight gain and increased relative liver weight in high-dose animals; increased cholesterol in high-dose males.	33.1 / 35.5	298 / 331	[redacted]. 1992, 1994 (amendment No. 3 including historical controls) (IUCLID 8.9.1.1-03
Rat (2-year)	Oral	Reduced body weight and body weight gain, signs of mild anaemia in females, gross necropsy and histopathological findings in the liver (both sexes) and the kidneys (males only) – in high dose group.	Chronic: 37 / 44 Carcinogenicity: 113 / 141	Chronic: 113 / 141 Carcinogenicity: - / -	[redacted]. (1993c). (IUCLID 8.9.1.1-07

Study and duration	Route	Relevant effects	NOAEL (mg/kg bw day) Males/females Parental/ offspring/reproduction* Maternal/developmental**	LOAEL (mg/kg bw day) Males/females Parental/ offspring/reproduction* Maternal/developmental**	References
Mouse (18-month)	Oral	Survival markedly reduced at 7000 ppm, body weight and body weight gain decreased from 5000 ppm, signs of anaemia at 7000 ppm, increased liver weight from 3000 ppm, bile duct hyperplasia at 7000 ppm (males), nephropathy from 5000 ppm.	Chronic: 112 / 133 Carcinogenicity: 851 / 1008	Chronic: 360 / 417 Carcinogenicity: - / -	[redacted]., (1993a & 1993b). (IUCLID 8.9.1.1-05 & 8.9.1.1-07)
Rat (2-generation study)	Oral	Decreased body weight and body weigh gain of parental rats and pups at 212 mg/kg bw/day. No reproductive effects.	*21 /21/ 212	*212 / 212/-	[redacted] 1992 (IUCLID 8.10.2-01)
Rat (developmental)	Oral	Dams: Reduced body weight gain and food consumption at 1000 mg/kg bw/day. Foetuses: No effects.	**100 / 1000	**1000 / -	[redacted]. 1989a (IUCLID 8.10.1-01)
Rabbit (developmental)	Oral	Dams: Reduced body weight gain at 100 mg/kg bw/day. Foetuses: No effects.	**100 / 300	**300 / -	[redacted]. 1989b (IUCLID 8.10.1-02)

12.1.2 Local effects

Fludioxonil is of low acute oral, dermal and inhalational toxicity. Fludioxonil is not irritating to the skin or the eye and has not been found to possess a skin sensitising potential. The product Sporgaard WB is not classified, based on specific product studies, for any local effects and risk assessment considerations regarding local effects are therefore not necessary.

12.1.3 Absorption

Route	Study	Test substance	Concentration of test substance	Applicability (concentration ranges)	Value
Oral	[redacted], 1990 (IUCLID 8.8.1-01)	Fludioxonil	Single and repeated low dose: 0.5 mg/kg bw Single high dose: 100 mg/kg bw	>80% (no correction necessary)	100%
Dermal	[redacted] 2005 (IUCLID 8.8.2-03)	Fludioxonil in SC formulation	0.05% & 23.3%	-	3% (used for both in use dilution and concentrate)
Inhalation	Study not performed	-	-	-	100% (default value)

12.2 REFERENCE VALUES

According to the Common Principles of Annex VI to Directive 98/8/EC, the establishment of an AEL should be based on an appropriate NOAEL: this is defined as the lowest relevant NOAEL in the most sensitive species in sub-acute and sub-chronic toxicity studies. However, the Expert Workshop on the Human Health Risk Characterisation of Biocides (2006) states that NOAELs from studies of various durations could be used as basis for the derivation of systemic Acceptable Exposure Levels (AELs) to cover acute, medium-term and long-term exposure. AEL values are therefore proposed in line with this guidance, in order to cover the various human exposure scenarios applied for.

12.2.1 Uncertainties and assessment factors

Fludioxonil is of low acute toxicity and is not mutagenic, teratogenic or a reproductive toxin. The critical effects from repeat-dose studies performed with fludioxonil are not considered likely to be relevant to a single exposure. No specific clinical signs or dead were attributed to dosing or other signs of toxic effects relevant for acute exposure in studies with relevant duration for this end point. It is notable that an Acute Reference Dose was not considered necessary for the listing of fludioxonil on Annex I of Directive 91/414/EEC, however it has formally been agreed to always set the three values and therefore the derivation of an AELacute/short-term is proposed below.

$AEL_{acute/short-term}$		
Uncertainty	**AF**	**Justification**
Interspecies variability	10	Toxicokinetic and toxicodynamic differences
Intraspecies variability	10	Toxicokinetic and toxicodynamic differences
Route to route extrapolation	1	
Time duration extrapolation	1	
NOAEL to LOAEL extrapolation	1	
Dose response	1	
Severity of key health effects	1	No genotoxicity, carcinogenicity, developmental or reproductive toxicity
Overall AF	**100**	

The rat and the dog are the most sensitive species for the liver effects and showed similar sensitivity based on similar NOAEL values from the 90 days studies ranging from 59-70 mg/kg/bw day.
Possible starting points for derivation of the $AEL_{acute/short-term}$ are the NOAEL of 100 mg/kg bw/d from the 28-day rat study (based on decreased weight gain and food consumption, clinical chemistry and increased liver weight); the NOAEL of 59 mg/kg bw/d from the 90-day dog study (based on decreased weight gain and food consumption, clinical chemistry, haematology, increased liver weight and pathology) or the NOAEL of 64 mg/kg bw/d from the the 90-day rat study (based on kidney and liver effects) ; the maternal and developmental NOAELs of 100 mg/kg bw/d from the rat developmental toxicity study; or the maternal NOAEL of 100 mg/kg bw/d from the rabbit developmental toxicity study.

The NOAEL from the 28-day rat study is also from the study of shortest duration, and is therefore more appropriate to use than the longer-term studies.
NOAELs from the developmental toxicity studies are also considered when deriving the acute AEL; however the relevance of the study findings should be taken into consideration. There is no evidence of developmental toxicity in either the rat or rabbit study. It it is gavage dosing studies which could give rise to Cmax related effects and considering that no developmental toxicity or teratogenicity were observed which is primarily the reasoning for using a maternal NOAEL, for AEL_{acute} or ARfD, based on e.g bw changes early in the study since any effects on the foetus can be considered as being caused by a single or few doses .Maternal toxicity in both of these studies was limited to reduced weight gain and food consumption. The maternal NOAEL for both developmental toxicity studies (100 mg/kg bw/d) is consistent with those derived for short-term repeated dose toxicity studies.

The majority of the ad hoc follow up group supported that the relevant NOAEL for deriving the AEL_{acute} was 100 mg/kg bw/d from the 28-day rat study. The members did not consider the rabbit developmental study in general suitable for deriving a reference value, and furthermore the effects on body weight gain observed at 100 mg/kg bw/d would not be appropriate for deriving AEL_{acute}.
An AELacute/short-term of 1 mg/kg bw is therefore derived, based on the NOAEL of 100 mg/kg bw/d from the 28 day oral rat study .
For comparison the LOAEL in the 90 days study dog study was 299 mg/kg bw day for similar effects with a NOAEL of 59 mg/kg bw day.

$AEL_{medium-term}$		
Uncertainty	**AF**	**Justification**
Interspecies variability	10	Toxicokinetic and toxicodynamic differences
Intraspecies variability	10	Toxicokinetic and toxicodynamic differences
Route to route extrapolation	1	
Time duration extrapolation	1	
NOAEL to LOAEL extrapolation	1	
Dose response	1	
Severity of key health effects	1	No genotoxicity, carcinogenicity, developmental or reproductive toxicity
Overall AF	**100**	

In the short- and long-term studies in the various animal species tested, the target organs identified are the liver, the kidneys, and the haematopoietic system. Fludioxonil is not considered to possess carcinogenic or genotoxic potential. It is not toxic to reproduction or a developmental toxicant.

The relevant starting point for the derivation of the fludioxonil medium-term AEL are the NOAEL values of 64 and 70 mg/kg bw/d (1000 ppm) in males and females, respectively from the 90-day rat study ([redacted], 1990a) and the NOAELs of 60.0 and 58.5 mg/kg bw/d (2000 ppm) in males and females, respectively from the 90-day dog study ([redacted], 1990). The similar NOAEL values indicate that the rat and dog are of comparable sensitivity to the toxicity of fludioxonil.
The NOAEL from the one-year dog study is not used as the difference in NOAEL's in the 90-day and one year study is considered to be due to difference in dose setting regime; LOAELs are comparable in the two studies.The results of the chronic mouse studies ([redacted], 1993a/b) give NOAELs of 300 and 417 mg/kg bw/d (3000 ppm) in males and females, respectively, indicating that mice are less sensitive to fludioxonil toxicity.

A medium term AEL of 0.59 mg/kg bw/d can therefore be derived for fludioxonil based on the lowest NOAEL of 58.5 mg/kg bw/d in the 90-day dog study and applying a standard assessment factor of 100 to account for potential inter-species and intra-species toxicokinetic and toxicodynamic differences. The use of a standard assessment factor is considered to be appropriate in the absence of any findings of genotoxicity, carcinogenicity, developmental or reproductive toxicity. Correction of this (systemic) AEL for the extent of oral absorption is not required as fludioxonil was found to be well absorbed (>80%) from the gastrointestinal tract in the rat ADME studies .

It is noted that the same derivation was used for the short-term systemic AOEL value for the use of fludioxonil in plant protection products (EFSA conclusion, 2007).

Although a 28-day dermal toxicity study is available for fludioxonil ([redacted] 1990; IIIA 8.9.1-02), the current guidance cautions against the use of route-specific AELs.

$AEL_{long-term}$		
Uncertainty	**AF**	**Justification**
Interspecies variability	10	Toxicokinetic and toxicodynamic differences
Intraspecies variability	10	Toxicokinetic and toxicodynamic differences
Route to route extrapolation	1	
Time duration extrapolation	1	
NOAEL to LOAEL extrapolation	1	
Dose response	1	
Severity of key health effects	1	No genotoxicity, carcinogenicity, developmental or reproductive toxicity
Overall AF	**100**	

Subchronic and chronic feeding studies indicate that repeated oral administration of Fludioxonil is toxic to the liver of rats, mice and dogs, and to the kidney of rats and mice.
Signs of hepatotoxicity include increased organ weight (relative to body weight in rats, mice and dogs) and histopathological changes (centrilobular hepatocyte hypertrophy in rats and mice in the short term studies; degeneration, atrophy, inflammation, and necrosis in rats in the long term study; bile duct hyperplasia in mice in the long term study; bile duct proliferation and portal fibrosis in dogs). An increased incidence of hepatocellular adenomas in high-dose female rats in the long term study is not considered to be related to the treatment with Fludioxonil.

Other target organs have also been identified in the short- and long-term studies including the kidney and the haematopoietic system. However, the effects observed in these two targets occurred at higher dose levels than the effects observed in the liver.

For all three tested species the liver is a target organ. The rat and the dog are the most sensitive species for the liver effects. There is no indication that the changes observed are not relevant for humans.

The relevant starting point for the derivation of the fludioxonil long-term AEL are the NOAELs of 18.9 and 21.1 mg/kg bw/d for males and females from the rat reproductive toxicity study ([redacted], 1992) and the NOAELs of 37 and 44 mg/kg bw/d from the chronic rat study [redacted], 1993c).
The lowest NOAEL from a dog study (58.5 mg/kg bw/d) and the lowest relevant NOAEL from a mouse study (360 mg/kg bw/d) indicate that these species are not of greater sensitivity. The NOAEL from the one-year dog study (33 mg/kg bw day) is not used as the difference in NOAEL's in the 90-day and one year study is considered to be due to difference in dose setting regime; LOAELs are comparable in the two studies."

Although the NOAEL from the rat reproductive toxicity study (18.9/21.1 mg/kg bw/d) is lower than that from the chronic study (37/44 mg/kg bw/d), this is a consequence of the dose spacing in these studies. The LOAEL for the chronic study (113/141 mg/kg bw/d) is lower than that the LOAEL from the reproductive study (213/237): the NOAEL from the chronic rat study is therefore the POD relevant to the derivation of the long-term AEL value.

A long-term AEL of 0.37 mg/kg bw/d can therefore be derived for fludioxonil, based on the NOAEL of 37 mg/kg bw/d from the chronic rat study and applying a standard assessment factor of 100. The use of a standard assessment factor is considered to be appropriate in the absence of any genotoxicity, carcinogenicity, developmental or reproductive toxicity.

It is noted that this derivation is the same as that used for the ADI value for the use of fludioxonil in plant protection products (EFSA conclusion, 2007).

12.2.2 Reference values to be used in Risk Characterisation

Reference	Study	NOAEL (LOAEL)	AF	Correction for oral absorption	Value mg/kg bw/day
$AEL_{acute/short-term}$	28 day oral rat study	100 (300)	100	>80% (no correction)	1
$AEL_{medium-term}$	90 day oral dog study	59 (299)	100	>80% (no correction)	0.59
$AEL_{long-term}$	2 year oral rat study	37 (113)	100	>80% (no correction)	0.37
ARfD	Not relevant				
ADI	Not relevant				

12.2.3 Maximum residue limits or equivalent

Human exposure to fludioxonil through the diet resulting from its use in biocidal preparations will be insignificant; it is therefore not necessary to propose or justify acceptable residues.
In addition to the above fludioxonil is not sprayed/applied on food and feedingstuffs and is unlikely to come into direct contact with food based on its use pattern.
Biocidal preparations of fludioxonil will not be used where food for human consumption is prepared, consumed or stored, or where animal foodstuff is prepared, consumed or stored.

Setting MRLs in food and feedstuffs is not considered necessary.

12.3 INDUSTRIAL USES

Exposure scenarios

This section considers exposures to fludioxonil which may occur in workers during scenarios where the biocidal product, Sporgard WB, is incorporated into end-use products (treated articles) such as paints (PT 7), industrial paper (PT 9) and masonry products (PT 10).
Sporgard WB may be added to end-use products during the formulation and manufacturing stages at industrial sites. The incorporation of the biocidal product into these end-use products takes place using closed and fully automated industrial processes and the potential for exposures to arise is very limited e.g. for less than a minute when connecting or disconnecting pipes or hoses using automated or semi-automated processes.

The finished end-use products incorporating the Sporgard WB biocide are then transported to professional users and retails stores.

Mixing and loading:

Adding concentrated preservative to paint during the manufacturing and formulation process.

The primary route of exposure associated with this task is the dermal route (inhalation exposures are considered to be negligible and ingestion is not expected). Industrial workers may be expected to handle the concentrated biocidal product 5 days/week, every week (more intermittent use may be expected in reality). This is considered to be a long-term exposure scenario and therefore the $AEL_{long\text{-}term}$ of 0.37 mg/kg bw/day has been used.

12.3.1 Systemic effects

Task/ Scenario	Tier I Tier II**	Systemic NOAEL mg/kg bw/d	AEL mg/kg bw/d	Estimated uptake* mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Mixing and loading phase: Industrial worker handling concentrate for PT7 (paint), PT9.02 (paper for drywall manufacture) & PT10 (gypsum powder/drywall manufacture) **RISKOFDERM – Loading liquid, automated or semi-automated (HEEG, 2008). Task duration 10 min** **Maintenace of machines (PT7-2)** Industrial worker conducting maintenance work done for the different parts of the production machines (used in paint manufacture and formulation) ECHA Biocides Guidance 2015: Biocides Human Health Exposure Methodology (dermal algorithm)						
PT7-1	I	37	0.37	1.0×10^{-2}	2.8	yes
	II	37	0.37	1.1×10^{-3}	0.3	yes
PT7-2	I	37	0.37	0.46	123.2	no
	II	37	0.37	4.6×10^{-2}	12.3	yes
PT9-1	I	37	0.37	1.0×10^{-2}	2.8	yes
	II	37	0.37	1.1×10^{-3}	0.3	yes
PT10-1	I	37	0.37	1.0×10^{-2}	2.8	yes
	II	37	0.37	1.1×10^{-3}	0.3	yes

*Estimated fludioxonil uptake.
**Tier II PPE = gloves (penetration 10%), coverall (penetration 20%); no RPE

Combined Exposure

Scenarios combined	Tier	Systemic NOAEL mg/kg bw/d	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Industrial workers: Mixing and loading/blending biocidal product into the paint (PT7-1) and maintenance activities (PT7-2)	I	37	0.37	0.47	127.0	No
Industrial workers: Mixing and loading/blending biocidal product into the paint (PT7-1) and maintenance activities (PT7-2)	II	37	0.37	$4.7x10^{-2}$	12.7	Yes

12.3.2 Local effects

Due to no classification for local effects of either the active substance or the product, based on specific product studies on Sporgard WB, there is no need to consider local effects separately.

12.3.3 Conclusion

Systemic exposures to fludioxonil in industrial workers associated with mixing and loading the Sporgard WB concentrate (containing up to 2% w/w fludioxonil) during the PT7 uses as paint manufacturing/formulating processes, PT9 uses as drywall paper manufacturing processes and PT10 uses as drywall gypsum manufacturing processes (e.g. connecting and disconnecting the concentrated product to the dosage pump via transfer lines) were determined using the default data in the HEEG *Opinion on the use of available data and models for the assessment of the exposure of operators during the loading of products into vessels or systems in industrial scale* (April 6, 2008) for liquid (semi-) automated transfer/pumping processes (the approach used is discussed in detail under section "8. Human exposure assessment"). A tiered approach was used, taking into account PPE, as appropriate.
The results of the risk assessment for systemic effects, takes into account a dermal absorption values of 3%.

Based on the predicted exposures and risk characterisation for systemic effects, acceptable risks were identified for industrial workers conducting maintenance work (PT7-2) done for the different parts of the production machines (used in paint manufacture and formulation) when wearing appropriate personal protective equipment PPE (gloves).
In the combined exposure scenario where the same industrial worker performs mix/load activities (PT7-1) and maintenance activities of production machines (PT7-2) in the same day acceptable use where obtained in Tier II (with gloves). These tasks are however expected to be carried out infrequently, e.g. once per year.

12.4 PROFESSIONAL USES

12.4.1 Systemic effects

12.4.1-1: Exposure scenarios for preserved film products (PT7)

Professional workers may be exposed to fludioxonil during the application of end-use products which have been preserved using Sporgard WB such as paints and mineral sealants and grouts (PT7) to give a maximum concentration up to 1.6% w/w of the biocidal product, equivalent to 0.032% w/w fludioxonil (based on a fludioxonil concentration of 2% w/w). The following tasks have been identified for professionals using preserved film products, PT7:

Mixing and loading (Sporgard WB exposure scenario):

Paints – mixing and loading is minimal

Application (Sporgard WB exposure scenario):

Spraying
Brush and roller
Applying mineral sealants and grouts

Post-application phase (Sporgard WB exposure scenario):

Cleaning out paint brushes after painting
Cleaning out spraying equipment after painting

The primary routes of exposure associated with these tasks are the dermal and the inhalation routes. Ingestion of the product during normal use is not expected. Unlike other more general painting products which could be applied daily by professional workers, it is expected that these fungicide-based products may be applied on 1-2 days per week or, less frequently (e.g. 1-2 days per month) however still resulting in many workdays per year and therefore considered to be repeated long-term exposures (which is also in line with other peer reviewed active substance in PT7 products). The exposure scenarios associated with these intended uses are therefore considered to be long-term exposure scenarios. The reference dose used in the risk characterisation is based on the NOAEL of 37 mg/kg bw/day from the 2-year rat study resulting in a $AEL_{long\text{-}term}$ of 0.37 mg/kg bw/day.

Task/ Scenario	Tier/PPE	Systemic NOAEL mg/kg bw/d	$AEL_{long-term}$ mg/kg bw/d	Estimated uptake** mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Application phase						
Scenario [PT7-3] Professionals applying preserved water-based paints by spraying (Sporgard WB max. 1.6% w/w). BEAT scenario: Spray application of masonry preservatives (remedial biocides). Task duration 360 min	**Tier 1** (gloves, no other PPE)	37	0.37	2.7×10^{-2}	7.4	Yes
	Tier 2a (gloves, coveralls, penetration = 20%; no RPE)	37	0.37	1.0×10^{-2}	2.8	Yes
	Tier 2b (gloves, coveralls, penetration = 20%; RPE: 10-fold protection)	37	0.37	5.5×10^{-3}	1.5	Yes
Scenario [PT7-4] Professional applying preserved water-based paints using a brush or roller (Sporgard WB max. 1.6% w/w). BEAT scenario: Indoors decorative painting (PT7) and Consumer Painting Mode l. Task duration 360 min	**Tier 1** (no PPE)	37	0.37	1.0×10^{-2}	2.8	Yes
	Tier 2 (PPE: gloves, penetration = 10%, coverall, penetration = 20%)	37	0.37	3.8×10^{-3}	1.0	Yes
Scenario [PT7-5] Professional applying preserved mineral sealants or grout (Sporgard WB max. 1.6% w/w) ConsExpo Model v.4.1 and RIVM DIY Product Factsheet: default scenario for joint	**Tier 1** (no PPE)	37	0.37	4.8×10^{-4}	0.13	Yes
	Tier 2 (gloves, 90% protection)	37	0.37	4.8×10^{-5}	0.01	Yes

Task/ Scenario	Tier/PPE	Systemic NOAEL mg/kg bw/d	$AEL_{long-term}$ mg/kg bw/d	Estimated uptake** mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
sealant, p.59 Task duration = 60 mins; worker remains in room for 480 mins						
Post-application phase						
Scenario [PT7-6] Professional washing out paint brushes after application (Sporgard WB max. 1.6% w/w) HEEG opinion 2008	**Tier 1** (no PPE)	37	0.37	2.8×10^{-5}	7.5×10^{-3}	Yes
	Tier 2 (gloves, penetration = 10%)	37	0.37	2.8×10^{-6}	7.5×10^{-4}	Yes
Scenario [PT7-7] Professional cleaning out spray equipment after application (Sporgard WB max. 1.6% w/w) BEAT indicative data Task duration 30 min	**Tier 1** (no PPE)	37	0.37	3.7×10^{-4}	0.1	Yes
	Tier 2 (PPE: gloves, penetration = 10%, coverall, penetration = 20%)	37	0.37	5.0×10^{-5}	0.01	Yes

Comparable dermal predicted exposures using ConsExpo silicon sealants model: Tier 1: 2.4 x 10-4; Tier 2: 2.4 x 10-5

***Estimated fludioxonil uptake*

Secondary (indirect) exposure scenarios

Task/ Scenario	**Tier/PPE**	**Systemic NOAEL** mg/kg bw/d	**$AEL_{long-term}$** mg/kg bw/d	**Estimated uptake*** mg/kg bw/d	**Estimated uptake/ AEL** (%)	**Acceptable** (yes/no)
Scenario [PT7-20] Professional worker sanding preserved paint or sealant. 6 hours/day (chronic exposure scenario)	**Tier 1**	37	0.37	6.1×10^{-2}	16.5	Yes

*Estimated fludioxonil uptake

Combined scenarios

Scenarios combined	Tier/PPE	Systemic NOAEL mg/kg bw/d	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Professionals – applying water-based paints by spraying (PT7-3), applying preserved mineral sealant or grout (PT7-5), and cleaning out spray equipment after use (PT7-7)	I (PPE: gloves for PT7-3)	37	0.37	$2.8x10^{-2}$	7.4	Yes
Professionals– applying water-based paints by spraying (PT7-3), applying preserved mineral sealant or grout (PT7-5) and cleaning out spray equipment (PT7-7)	II (IIa for PT7-3)	37	0.37	$1.0x10^{-2}$	2.7	Yes
Professionals– applying water-based paints by spraying (PT7-3), applying preserved mineral sealant or grout (PT7-5), and cleaning out spray equipment (PT7-7)	II(IIb for PT7-3)	37	0.37	$5.6x10^{-3}$	1.5	Yes
Professional– applying water-based paints using a brush or a roller (PT7-4), applying mineral sealant or grout (PT7-5), and washing out paint brushes (PT7-6)	I	37	0.37	$1.1x10^{-2}$	2.9	Yes
Professional– applying water-based paints using a brush or a roller (PT7-4), applying mineral sealant or grout (PT7-5), cutting/sawing or drilling gypsum drywall (PT10-2)	II	37	0.37	$3.9x10^{-3}$	1	Yes

and washing out paint brushes (PT7-6)						

12.4.1-2: Exposure scenarios for preserved materials (PT9)

There are no direct professional uses of drywall coating paper which has been treated with Sporgard WB as a preservative. The treated drywall coating paper is used to manufacture drywall (e.g. plasterboard) end-use products which may be used by professional workers during construction tasks. A risk characterisation for the use of drywall products is described under the use of preserved masonry (PT10) below.

12.4.1-3: Exposure scenarios for use of preserved masonry materials (PT10)

Sporgard WB is used to treat gypsum plaster used in drywalls (e.g. plasterboard, wallboard or gypsum board) to prevent fungal growth. The gypsum plaster is pressed between two thick sheets of paper. Drywall is used to make interior walls and ceilings. The biocidal product is directly incorporated into the gypsum powder at the time of manufacture. Drywall products may be used by professional builders during construction tasks who may cut, saw or drill them using power tools. Mixing and loading, and post-application phases are not relevant. Exposure may arise during the application of the products (e.g. cutting to size or fixing to structures using a drill).

Sporgard WB is incorporated as a preservative in gypsum powder at concentrations up to 1.6% w/w, giving maximum concentrations of fludioxonil of 0.032% respectively (Sporgard WB contains the active substance, fludioxonil at 2% w/w). The following tasks have been identified for professionals using preserved masonry products, PT10.

Application:

Cutting, sawing or drilling drywall during construction tasks using power tools.

The primary routes of exposure associated with these tasks are the dermal and the inhalation routes. Ingestion of the product during normal use is not expected. Professional workers may be expected to handle the preserved products 5 days/week, every week (more intermittent use may be expected in reality). These are considered to be **long-term exposure scenarios**. The reference dose used in the risk characterisation is based on the NOAEL of 37 mg/kg bw/day from the 2-year rat study resulting in a $AEL_{long\text{-}term}$ of 0.37 mg/kg bw/day.

Task/ Scenario	**Tier/PPE**	**Systemic NOAEL** mg/kg bw/d	**$AEL_{long\text{-}term}$** mg/kg bw/d	**Estimated uptake*** mg/kg bw/d	**Estimated uptake/ AEL** (%)	**Acceptable** (yes/no)
Scenario [PT10-2]	Tier 1 (no PPE)	37	0.37	8.0×10^{-5}	0.02	Yes
Professionals cutting/sawing or drilling gypsum drywall ECETOC TRA V3 model – workers	Tier 2 (gloves, 90% effectiveness)	37	0.37	5.1×10^{-5}	0.01	Yes

*Estimated fludioxonil uptake

Combined scenarios

Combined exposure scenario relevant to PT10 uses have been addressed in section 12.4.1-1: It is envisaged that professional workers (e.g. decorators) may conduct tasks which involve handling various professional products which have been preserved using Sporgard, and hence combined exposures have been considered for PT7 and PT10 uses.

12.4.2 Local effects

Due to no classification for local effects of either the active substance or the product, based on specific product studies on Sporgaard WB, there is no need to consider local effects separately.

12.4.3 Conclusion

Preserved film products (PT7)

Systemic exposures to fludioxonil in professional workers associated with mixing and loading, and applying end-use products preserved using Sporgard WB (containing up to 2% w/w fludioxonil) and cleaning equipment after use were determined using default scenarios in the EU TNsG, the HEEG opinion, ECETOC TRA model or the BEAT model (the approaches used are discussed in detail in the corresponding Document IIB). Separate calculations for the mixing and loading phase have not been carried out since potential exposures are already accounted for in default data for the application phase. A tiered approach was used, taking into account PPE, as appropriate.

The results of the risk assessment for systemic effects, takes into account a dermal absorption values of 3%.
Based on the predicted exposures and risk characterisation for systemic effects, tasks involving the uses of end-use film products preserved using Sporgard WB carried out by professional workers are not considered to pose an unacceptable risk to human health neither with and without PPE.

Preserved materials (PT9)
There are no direct professional uses of drywall coating paper which has been treated with Sporgard WB as a preservative.

Preserved masonry materials (PT10)
Based on the predicted exposures and risk characterisation for systemic effects, tasks involving the use of preserved masonry products carried out by professional workers are not considered to pose an unacceptable risk to human health.

12.5 NON-PROFESSIONAL USERS

12.5.1 Systemic effects

12.5.1-1: Exposure scenarios for preserved film products (PT7)

Non-professionals (consumers) may be exposed to Sporgard WB when using preserved paints, sealants or grouts for DIY tasks. These products may be applied using a low/medium pressure sprayer, a brush or a roller or an application tool such as a trowel depending on the application. Products are ready-mixed. After application, equipments may be cleaned. These products are preserved using Sporgard WB (containing up to 2% w/w fludioxonil) at concentrations up to 1.6%.

The following tasks have been identified for consumers using preserved film products, PT7.

<u>Mixing and loading (Sporgard WB exposure scenario):</u>

Paints – mixing and loading is minimal

Application (Sporgard WB exposure scenario):

Spraying,
Brush and roller
Applying sealants and grouts (mineral)

Post-application phase (Sporgard WB exposure scenario):

Cleaning out paint brushes after painting
Cleaning out spraying equipment after painting

The primary routes of exposure associated with these tasks are the dermal and the inhalation routes. Ingestion of the product during normal use is not expected. Consumers may typically carry out these tasks on 2 to 5 consecutive days, once a year. This is considered to be a **short-term exposure scenario**.
The reference dose used in the risk characterisation is based on the NOAEL of 100 mg/kg bw/day from the 28 day rat study resulting in a $AEL_{short\text{-}term}$ of 1 mg/kg bw/day.

Systemic exposures to fludioxonil in consumers when applying end-use products preserved using Sporgard WB (containing up to 2% fludioxonil) and cleaning equipment after use were determined using default scenarios in the EU TNsG, the HEEG opinion, ECETOC TRA model or or ConsExpo v.4.1 and the corresponding RIVM Factsheets (the approaches used are discussed in details in the corresponding Doc IIB). Separate calculations for the mixing and loading phase have not been carried out since potential exposures are already accounted for in the default data for the application phase. A tiered approach was used, taking into account PPE, as appropriate.
The results of the risk assessment for systemic effects, takes into account a dermal absorption values of 3%.

Task/ Scenario	Tier/PPE	Systemic NOAEL mg/kg bw/d	$AEL_{short-term}$ mg/kg bw/d	Estimated uptake* mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Application phase						
Scenario [PT7-8] Non-professionals applying preserved water-based paints by spraying (Sporgard WB max. 1.6% w/w) Consumer Product Spraying and Dusting Model 3 – medium pressure spraying. Task duration 40 min	**Tier 1** (no PPE)	100	1	2.4×10^{-3}	0.24	Yes
Scenario [PT7-9] Non-professionals applying preserved water-based paints using a brush/roller (Sporgard WB max. 1.6% w/w) BEAT scenario: Indoor decorative painting (PT7) and Consumer Painting Model 1. Task duration 150 min	**Tier 1** (no PPE)	100	1	5.8×10^{-4}	5.8×10^{-2}	Yes
Scenario [PT7-10] Non-professional applying preserved mineral sealant or grout (Sporgard WB max. 1.6% w/w) ConsExpo v.4.1 and RIVM DIY Products Factsheet: default scenario for joint sealant p.	**Tier 1** (no PPE)	100	1	2.4×10^{-4}	2.4×10^{-2}	Yes

Task/ Scenario	**Tier/PPE**	**Systemic NOAEL** mg/kg bw/d	**$AEL_{short-term}$** mg/kg bw/d	**Estimated uptake*** mg/kg bw/d	**Estimated uptake/ AEL** (%)	**Acceptable** (yes/no)
59 1 event/day; Task duration 30 min						
Post-application phase						
Scenario [PT7-11] Non-professional washing out paint brushes after application (Sporgard WB max. 1.6 % w/w). HEEG opinion 2008	**Tier 1** (no PPE)	100	1	2.8×10^{-5}	2.8×10^{-3}	Yes
Scenario [PT7-12] Non-professional cleaning out spray equipment after application (Sporgard WB max. 1.6% w/w) BEAT indicative data Task duration 30 min	**Tier 1** (no PPE)	100	1	3.7×10^{-4}	3.7×10^{-2}	Yes

*Estimated fludioxonil uptake

Secondary (indirect) exposure scenarios

Task/ Scenario	Tier/PPE	Systemic NOAEL mg/kg bw/d	$AEL_{short-term}$ mg/kg bw/d	Estimated uptake* mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Scenario [PT7-21] Non-professional (consumer) sanding preserved paint or sealant. 1 hour/day (acute exposure scenario)	**Tier 1**	100	1	1.0×10^{-2}	1.023	Yes

*Estimated fludioxonil uptake

Combined scenarios

Scenarios combined	Tier	Systemic NOAEL mg/kg bw/d	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake*/ AEL (%)	Acceptable (yes/no)
Non-professionals – applying water-based paints by spraying (PT7-8), applying preserved mineral sealant or grout (PT7-10) and cleaning out spray equipment after use (PT7-12)	I	100	1	2.7×10^{-3}	0.3	Yes
Non-professionals – applying preserved water-based paints using brush and roller (PT7-9), applying mineral sealant or grout (PT7-10) and washing out paint brushes (PT7-11)	I	100	1	8.5×10^{-4}	8.5×10^{-2}	Yes

12.5.1-2: Exposure scenarios for preserved materials (PT9)

There are no non-professional uses envisaged for preservatives which are used to treat industrial paper (PT9.02) as these are incorporated into articles during the formulation/manufacturing stage. Risk assessments are therefore not required.

12.5.1-3: Exposure scenarios for use of preserved masonry materials (PT10)

Non-professionals (consumers) may be exposed to fludioxonil when using drywall products containing gypsum power which has been treated with Sporgard WG to prevent fungal growth. Consumers may use power tools to cut, saw or drill drywall during DIY construction tasks. Sporgard WG is incorporated as a preservative in gypsum powder at concentrations up to 1.6 % w/w; giving maximum concentrations of fludioxonil of 0.032% w/w (Sporgard WB contains fludioxonil at 2% w/w). The following tasks have been identified for consumers using preserved masonry products, PT10.

Application
Cutting, sawing or drilling drywall during construction tasks using power tools
The primary routes of exposure associated with this task are the dermal and the inhalation routes. Ingestion of the product during normal use is not expected. Consumers may typically carry out these tasks on 2 to 5 consecutive days, once a year. This is considered to be a short-term exposure scenario.

Systemic exposures to fludioxonil in consumers when cutting, sawing or drilling drywall preserved using Sporgard (containing up to 2% w/w fludioxonil) during construction tasks was assessed using default scenarios in the ECETOC TRA model. A tiered approach was used, taking into account PPE, as appropriate. The results of the risk assessment for systemic effects, takes into account a dermal absorption values of 3%.

Task/ Scenario	Tier/PPE	Systemic NOAEL mg/kg bw/d	$AEL_{short-term}$ mg/kg bw/d	Estimated uptake* mg/kg bw/d	Estimated uptake (fludioxonil)/ AEL (%)	Acceptable (yes/no)
Application phase						
Scenario [PT10-3] *Non-professionals cutting/sawing or drilling gypsum drywall (Sporgard max. 1.6% w/w) ECETOC TRA V3 model*	**Tier 1** (no PPE)	100	1	3.6×10^{-5}	3.6×10^{-3}	Yes

*Estimated fludioxonil uptake

Combined scenarios
Combined exposure scenario relevent to PT10 uses have been addressed in section 12.5.1-1: It is envisaged that consumers may conduct tasks which involve handling various DIY products which have been preserved using Sporgard, and hence combined exposures have been considered for PT7 and PT10 uses.

12.5.2 Local effects

Due to no classification for local effects of either the active substance or the product, based on specific product studies on Sporgaard WB, there is no need to consider local effects separately.

12.5.3 Conclusion

Preserved film products (PT7)
Based on the predicted exposures and risk characterisation for systemic effects, tasks involving the uses of end-use film products preserved using Sporgard WB carried out by non-professionals are not considered to pose an unacceptable risk to human health.

Preserved materials (PT9)
There are no direct professional uses of drywall coating paper which has been treated with Sporgard WB as a preservative.

Preserved masonry materials (PT10)
Based on the predicted exposures and risk characterisation for systemic effects, tasks involving the uses of preserved masonry products carried out by consumers are not considered to pose an unacceptable risk to human health.

12.6 SECONDARY (INDIRECT) EXPOSURE AS A RESULT OF USE

(GENERAL PUBLIC)

12.6.1 Systemic effects

12.6.1-1: Exposure scenarios for preserved film products (PT7)

Potential indirect exposures to fludioxonil from products (PT7) preserved using Sporgard WB may arise during the following scenarios:

- Child/adult touching a wet or dried painted surface and mouthing
- An adult washing out contaminated coveralls
- Child/adult touching the preserved materials (e.g. mineral sealants or fillers)

Non-users, for example a child or infant, may be exposed when touching a painted surface before the paint (preserved using Sporgard WB) has dried. The child is unlikely to touch the surface more than once: this is considered to be an **acute/short-term exposure scenario**.
Indirect, secondary exposures to fludioxonil may arise when adults are washing out contaminated coveralls after spraying paint (preserved using Sporgard WB), e.g. after 2 days of use. Coveralls may be washed weekly, after 5 days of wear. This is considered to be a **medium-term exposure scenario**.
Secondary, indirect exposures to fludioxonil can arise when a child or infant touches wet mineral sealant which has been applied to a surface before this has dried. Since consumers use these products infrequently (e.g. 1-2 times per year), this is considered to be a **acute/short-term exposure scenario**. The reference dose used in the risk characterisation is based on the NOAEL of 100 mg/kg bw/day from the 28 day rat study resulting in a $AEL_{acute/short-term}$ of 1 mg/kg bw/day.

Indirect systemic exposures to fludioxonil in toddlers and adults arising from contact with end-use products preserved using Sporgard WB (i.e. touching a wet painted surface or sealant) or with contaminated articles (i.e. overalls from paint spraying) were determined using default scenarios from TNsGs on Human Exposure, Part 3 and HEEG Opinion on Default human factors values for use in exposure assessments for biocidal products (2013). The results of the risk assessment, takes into account a dermal absorption values of 3%.

Task/ Scenario	Tier/PPE	Systemic NOAEL mg/kg bw/d	$AEL_{short-term}$ mg/kg bw/d	Estimated uptake* mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Scenario [PT7-13] Toddler-touching wet painted surface Recommendation No. 5 of the BPC Ad hoc Working Group on Human Exposure: Non-professional use of antifouling paints: exposure assessment for a toddler	Not relevant	100	1	1.3×10^{-3}	0.13	Yes
Scenario [PT7-14] Toddler-touching wet painted surface and mouthing Recommendation No. 5 of the BPC Ad hoc Working Group on Human Exposure: Non-professional use of antifouling paints: exposure assessment for a toddler	Not relevant	100	1	5.6×10^{-3}	0.56	Yes
Scenario [PT7-15] Toddler touching dried painted surface Recommendation No. 5 of the BPC Ad hoc Working Group on	Not relevant	100	1	5.6×10^{-5}	5.6×10^{-3}	Yes

Task/ Scenario	**Tier/PPE**	**Systemic NOAEL** mg/kg bw/d	**$AEL_{short-term}$** mg/kg bw/d	**Estimated uptake*** mg/kg bw/d	**Estimated uptake/ AEL** (%)	**Acceptable** (yes/no)
Human Exposure: Non-professional use of antifouling paints: exposure assessment for a toddler						
Scenario [PT7-16] Toddler touching dried painted surface and mouthing Recommendation No. 5 of the BPC Ad hoc Working Group on Human Exposure: Non-professional use of antifouling paints: exposure assessment for a toddler	Not relevent	100	1	1.0×10^{-3}	0.1	Yes
Scenario [PT7-17] Adult-laundry of contaminated coveralls after paint spraying activities	Not relevant	59	0.59**	7.6×10^{-4}	0.13	Yes
Scenario [PT7-18] Toddler-dermal contact with wet preserved materials (e.g mineral sealants and grouts)	Not relevant	100	1	2.2×10^{-4}	2.2×10^{-2}	Yes
Scenario [PT7-19] Toddler-dermal contact with wet preserved	Not relevant	100	1	9.4×10^{-4}	9.4×10^{-2}	Yes

Task/ Scenario	**Tier/PPE**	**Systemic NOAEL** mg/kg bw/d	**$AEL_{short-term}$** mg/kg bw/d	**Estimated uptake*** mg/kg bw/d	**Estimated uptake/ AEL** (%)	**Acceptable** (yes/no)
materials (e.g mineral sealants and grouts) and mouthing						
Scenario (screening) Long term inhalation exposure for volatilised residues.	Not relevant	8.6×10^{-5}	Not relevant	Not relevant	Not relevant	Yes

*Estimated fludioxonil uptake (systemic)

** compared with $AEL_{medium-term}$=0.59 mg/kg/bw day

Combined scenarios

There are no combined scenarios for secondary exposures.

12.6.2 Local effects

Due to no classification for local effects of either the active substance or the product, based on specific product studies on Sporgaard WB, there is no need to consider local effects separately.

12.6.3 Conclusion

Preserved film products (PT7)
Based on the predicted exposures and risk characterisation for systemic effects, potential indirect exposures arising from the uses of preserved film products are not considered to pose an unacceptable risk to human health.

Preserved materials (PT9)
There are no indirect exposure scenarios associated with the use of preserved materials (PT9).

Preserved masonry materials (PT10)
There are no indirect exposure scenarios associated with the use of preserved masonry (PT10).

12.7 INDIRECT EXPOSURE VIA FOOD

Human exposure to fludioxonil through the diet resulting from its use in biocidal preparations is considered insignificant; it is therefore not necessary to propose or justify acceptable residues.
Fludioxonil is not sprayed/applied on food and feedingstuffs and is unlikely to come into direct contact with food based on its use pattern.
Biocidal preparations of fludioxonil will not be used where food for human consumption is prepared, consumed or stored, or where animal foodstuff is prepared, consumed or stored.

12.8 PRODUCTION / FORMULATION OF ACTIVE SUBSTANCE

Potential exposures during the manufacture of the active substance and its formulation into the biocidal product are considered under The Chemical Agents at Work Directive (98/24/EC, within 89/391/EEC) and are 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. These regulations competently control for operator exposure to the biocides and substance of concern in the paint formulation.

13 RISK CHARACTERISATION FOR THE ENVIRONMENT

In the following environmental risk characterisation, risk quotients (PEC/PNEC relationships) are calculated for the active compound fludioxonil and its degradation products. For the exposure assessment a tonnage based approach has been used for the formulation phases of PT7, 9 and 10 (scenario 1, 4 and 5). Additionally a consumtion based approach has been applied for the formulation phase of PT9 according to the ESD PT6, 7 and 9 (scenario 3). For the application and service life of the paint (indoor use (PT7)) a tonnage based approach is applied (scenario 2a) according to the scenario in ESD PT7 and a consumption based approach is applied for the application and service life of sealant (indoor use (PT7)) in scenario 2b according to the city scenario. For the application phase and service life of the end-use products in PT9 and 10 no environmental emissions will occur and therefore no calculations are performed.
Calculated PEC/PNEC values for the tonnage based approach can be found in the *confidential* Appendix III.
The calculated PEC/PNEC values for the STP, the aquatic and the terrestrial compartment are compared with the trigger value of 1. If the PEC/PNEC value is equal to or below 1, this is interpreted as an acceptable risk to the environment. As explained in the CAR (Section 4.2.8 Ecotoxicity of relevant photo-degradation products) then the degradation products are less toxic than fludioxonil and will therefore be covered by the effect assessment of fludioxonil, it is found that this conclusion is applicable for organisms in all the environmental compartments that are assessed. In the following PNEC values for fludioxonil will therefore be used for the risk assessment of the degradation values as a worst case.

Fludioxonil

In the Table below PEC/PNEC values are calculated for fludioxonil for the relevant scenarios. Calculted PEC/PNEC values for the tonnage based approach can be found in the *confidential* Appendix III.

Summary table on calculated PEC/PNEC values for fludioxonil					
	PEC/PNEC$_{STP}$	**PEC/PNEC$_{water}$**	**PEC/PNEC$_{sed}$**	**PEC/PNEC$_{soil30d}$**	**PEC$_{GW}$/max limit** Agr. soil
PT7					
Industrial use *Scenario 1* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *Scenario 2a* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *Scenario 2a* *Consumption*	8.52×10^{-5}	6.63×10^{-4}	0.0457	0.0299	4.31×10^{-3}
PT9					
Industrial form. *Scenario 3* *Consumption*	0	0	0	0	0
Industrial use. *Scenario 4* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *No emission*	0	0	0	0	0
PT10					

Summary table on calculated PEC/PNEC values for fludioxonil					
	PEC/PNEC$_{STP}$	**PEC/PNEC$_{water}$**	**PEC/PNEC$_{sed}$**	**PEC/PNEC$_{soil30d}$**	**PEC$_{GW}$/max limit** Agr. soil
Industrial use *Scenario 5* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *No emission*	0	0	0	0	0
Aggregated risk					
Aggregated risk	<1.0	<1.0	<1.0	<1.0	<1.0

Degradation products in water

The major photo-degradation products (>10% applied fludioxonil) in the water phase are identified as CGA 339833 (max. 30.5%), CGA 344623 (max. 12.4%) and A5 (max 11.5%). In the Table below PEC/PNEC values are calculated for these photo-degradation products in the water and sediment phase. PNEC values for fludioxonil are used as a worst case. Calculted PEC/PNEC values for the tonnage based approach can be found in the *confidential* Appendix III.

Summary table on calculated water and sediment PEC/PNEC values for CGA 339833, CGA 344623 and A5						
	PEC/PNEC$_{water}$	**PEC/PNEC$_{sed}$**	**PEC/PNEC$_{water}$**	**PEC/PNEC$_{sed}$**	**PEC/PNEC$_{water}$**	**PEC/PNEC$_{sed}$**
PT7	**CGA 339833**		**CGA 344623**		**A5**	
Industrial use *Scenario 1* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *Scenario 2a* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and	2.54×10^{-4}	5.56×10^{-6}	9.88×10^{-5}	2.18×10^{-6}	7.84×10^{-5}	2.16×10^{-6}

service life *Scenario 2b* *Consumption*						
PT9						
Industrial form. *Scenario 3* *Consumption*	0	0	0	0	0	0
Industrial use *Scenario 4* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *No emission*	0	0	0	0	0	0
PT10						
Industrial use *Scenario 5* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *No emission*	0	0	0	0	0	0
Aggregated risk						
Aggregated risk	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0

Degradation products in soil

The major photo-degradation products (>10% applied fludioxonil) in the soil phase are identified as CGA 339833 (max. 9.1%), CGA 192155 (max. 11.7%) and CGA 265378 (max 12.3%). In the Table below PEC/PNEC values are calculated for these photo-degradation products in the soil and groundwater phase. The PNECsoil value for fludioxonil is used as a worst case. For groundwater the max limit of 0.1 µg/L is applied to the worst case calculated value from FOCUS PEARL 4.4.4. Calculted PEC/PNEC values for the tonnage based approach can be found in the *confidential* Appendix III.

Summary table on calculated soil and refined groundwater PEC/PNEC values for CGA 339833, CGA 192155 and CGA 265378						
	PEC/PNEC$_{soil30d}$	**Refined PEC$_{GW}$/max limit** Agr. soil	**PEC/PNEC$_{soil30d}$**	**Refined PEC$_{GW}$/max limit** Agr. soil	**PEC/PNEC$_{soil30d}$**	**Refined PEC$_{GW}$/max limit** Agr. soil
PT7	**CGA 339833**		**CGA 192155**		**CGA 265378**	
Industrial use *Scenario 1* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *Scenario 2a* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *Scenario 2b* *Consumption*	3.42×10^{-3}	<1.0	2.83×10^{-3}	<1.0	4.12×10^{-3}	<1.0
PT9						
Industrial form. *Scenario 3* *Consumption*	0	0	0	0	0	0
Industrial use *Scenario 4* Tonnage	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0
Private use and service life *No emission*	0	0	0	0	0	0
PT10						
Industrial use *Scenario 5* *Tonnage*	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0

Private use and service life *No emission*	0	0	0	0	0	0
Aggregated risk						
Aggregated risk	<1.0	<1.0	<1.0	<1.0	<1.0	<1.0

13.1 ATMOSPHERE

Fludioxonil has a low vapour pressure of 3.9 x 10^{-7} Pa (at 25ºC) and a low Henry's law constant of ca. 5.4 x 10^{-5} m^3 Pa mol^{-1}. Therefore, volatilisation from soil or water is not expected to be a significant entry route into air for fludioxonil. Based on Atkinson calculation (Stamm, 1999; IUCLID 10.3.1-01), standard conditions, 5 x 10^5 OH radicals/cm^3, 24 hour day, the photochemical oxidative degradation in air would proceed with a half-live of 6.7 hours (3.6 hours for a 12 hour day, 1.5 x 10^6 OH radicals/cm^3).

Conclusion: **Referring to these results, an accumulation of fludioxonil in air is not expected.**

13.2 SEWAGE TREATMENT PLANT (STP)

The exposure pathway for each of the five scenarios results in a direct emission to the sewage treatment plant. In the sewage treatment plant the main part of fludioxonil sorbs to the sludge (87.6%) while a minor part stays in the water phase (12.4%). Only 2.45 x 10^{-6}% evaporates. Fludioxonil is not very toxic for the activated sludge ($PNEC_{stp}$ = 0.18 mg/L)

Conclusion: **The results in the tables above show that the requirements for acceptable risk in sewage treatment plant are met for all the single uses of fludioxonil (covering also the degradation products) as well as for the aggregated risk.**

13.3 AQUATIC COMPARTMENT

Fludioxonil is stable to hydrolysis at environmentally relevant pH values and temperature, but is readily degraded by photolysis in aqueous solution, with a first order half-life equivalent to 9.3 days of natural sunlight. The major photo-degradation products (>10% applied fludioxonil) are identified as CGA 339833 (max. 30.5%), CGA 344623 (max. 12.4%) and A5 (max 11.5%). Fludioxonil is not readily biodegradable and therefore is not expected to be degraded in biotic systems. However, fludioxonil will rapidly dissipated from the water phase in water/sediment systems (DT_{50} water = 1 to 2 days) due to rapid adsorption to the sediment. Degradation in the whole water sediment system is slow, with a first order DT_{50} value in the range 451-699 days (20 °C). Fludioxonil is quite toxic to aquatic organisms with a $PNEC_{freshwater}$ = 0.0019 mg/L and a $PNEC_{sediment}$ = 0.40 mg/kg dry sediment (0.0870 mg/kg wet sediment)

Conclusion:

Freshwater: **The results in the tables above show that the requirements for acceptable risk in surface water are met for all the single uses of fludioxonil (covering also the degradation products) as well as for the aggregated risk.**

Sediment: **The results in the tables above show that the requirements for acceptable risk in sediment are met for all the single uses of fludioxonil (covering also the degradation products) as well as for the aggregated risk.**

13.4 TERRESTRIAL COMPARTMENT

Fludioxonil exhibits a low potential for mobility in soil with a mean K_{aoc} = 145,000 L/kg, no significant influence of the pH is observed. Fludioxonil is slightly degradable in soil in the dark, with CO_2 and bound residues the principal degradation products. The rate of degradation of fludioxonil in soil under dark aerobic conditions at 20 °C is in the range of 143 to 482 days (geo. Mean of 502 days at 12 °C). In the

dark at 25 °C under anaerobic conditions the degradation rate of fludioxonil is equally slow (DT_{50} >1 year).
Photolysis represents the major pathway of degradation for fludioxonil on soil surfaces with a degradation rate of 27 days (12 °C). The major soil photolysis products formed are CGA 339833 (max 9.1%), CGA 192155 (max 11.7%) and CGA 265378 (max 12.3%). Experimental data for CGA 339833 and CGA 192155 indicate that these metabolites are readily degraded in soil and will not persist.

Conclusion: **The results in the tables above show that the requirements for acceptable risk in soil are met for all the single uses of fludioxonil (covering also the degradation products) as well as for the aggregated risk.**

13.5 GROUNDWATER

Conclusion:

Fludioxonil has a very high Koc and is very unlikely to reach the groundwater compartment. The porewater values calculated are below 0.1 µg/L and as such indicate no risk to groundwater for all the scenarios.

The soil photodegradation products, CGA339833, CGA192155 and CGA265378 have low Koc values and were calculated to occur in groundwater at above 0.1 µg/L. However, higher tier modelling of the degradation products was conducted with FOCUS PEARL 4.4.4, which indicated that the photodegradation products would not occur in groundwater at levels above 0.1 µg/L in all the scenarios considered together. Consequently, no risk to groundwater is expected.

13.6 PRIMARY AND SECONDARY POISONING

Conclusion:

No primary poisoning is foreseen for the product.

According to the guidance (REACH R16, point R16.6.7), a detailed assessment of secondary poisoning is required if a substance has a bioaccumulation potential, and is neither readily biodegradable nor hydrolysable, and may also cause toxic effects if accumulated in higher organisms. Based on this assessment, consideration of the secondary poisoning exposure route is not found relevant for fludioxonil.

13.7 AGGREGATED EXPOSURE (COMBINED FOR RELEVANT EMMISSION SOURCES)

Calculations for aggregated risk have been performed as all emissions are discharged via sewage treatment plant. Calculations and conclusions are found in the above sections. No aggregated risk is found for any environmental compartment when considering all the uses together eventhough several of the uses will not occur at different locations and therefore be separate in time and space and the opportunity for aggregated exposure is limited.

When considering the treated article, gypsum plates, then both PT9 and PT10 uses are included in the final treated article. It could therefore be argued that PT9 and PT10 should be evaluated together. When considering PT9 and PT10 together by adding PEC/PNEC values from scenario 4 with those for scenario 5 then a safe risk is found.

14 RISK CHARACTERISATION FOR THE PHYSICO-CHEMICAL PROPERTIES

Sporgard WB is a yellow, faintly aromatic, moderately viscous liquid. Tests have shown Sporgard WB not to be explosive, oxidising or flammable and as such the product will not require labelling for physical chemical hazard. Sporgard WB has a pH of 6.5 and is chemically and physically stable when stored at 20°C and 50% relative humidity and has no reaction with stainless steel or non-fluorinated HDPE containers. The product shelf-life is expected to be at least 2 years.

15 MEASURES TO PROTECT MAN, ANIMALS AND THE ENVIRONMENT

Recommended methods and precautions concerning handling, use, storage, transport or fire	Handling and storage: When using do not eat, drink or smoke If swallowed seek medical advice immediately and show the container or label. This material and its container must be disposed of as hazardous waste. Avoid release to the environment. Keep away from food, drink and animal feed stuffs. Transport: Not regulated Fire: Not flammable, danger of toxic gases in smoke in case of fire (carbon, fluor and nitrogen oxides). Recommended fire-fighting media: foam, carbon dioxide, dry powders, spray water. Avoid the escape of the fire-fighting water to the environment. Wear a self-contained breathing apparatus. Combustion gases: In the event of fire, the formation of carbon monoxide and nitrogen and flour oxides must be anticipated.
Emergency measures in case of an accident	**a. Environmental precautions and methods of cleaning up:** Prevent entry into drains, water or soil. Recover the product by pumping, suction or absorption using dry and insert absorbed clay, dry sand or earth. Shovel up and place into a labelled tightly closed container. To clean contaminated floors and objects, wipe with a damp cloth. All contaminated cleaning materials should be placed in closable receptacle. Dispose of safely in a suitable sewage plant or incinerated **b. Methods of decontamination of water in case of an accident** In case of contamination of water with fludioxonil, always try to isolate and protect the contaminated area. Where feasible, the contaminated water can be pumped out and then isolated for further treatment as appropriate. If accidentally contaminated water is normally used to protect drinking water, contact the competent authorities
Possibility of destruction or decontamination following release in or on the following: (a) air (b) water, including drinking water (c) soil	Controlled incineration is the preferred means to safely dispose of the active substance as well as the products containing it, contaminated materials or packaging.
Procedures for waste management of the active substance for industry or professional users	**Product:** Recover the product by damping then sweeping or suction **Package product wastes:** Close and label the waste receptacles and dispose of, likewise any unclean empty containers. Dispose of them at a suitable waste incineration plant in accordance with the official regulations. Where large quantities are concerned, consult the supplier.

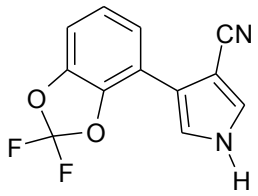
Part D: Appendices

Appendix I: List of endpoints

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

Active substance (ISO Name)	Fludioxonil
Product-type	PT 7, 9, 10

Identity

Chemical name (IUPAC)	4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1H-pyrrole-3-carbonitrile
Chemical name (CA)	4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1H-pyrrole-3-carbonitrile
CAS No	131341-86-1
EC No	No entry
Other substance No.	CIPAC no. 522
Minimum purity of the active substance as manufactured (g/kg or g/l)	950 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	sodium 4-toluene sulphonate (SYN549410) (max. 5 g/kg) of toxicological relevance 1-[2-cyano-1-(2,2-difluoro-1,3-benzodioxol-4-yl)ethyl]-4-(2,2-difluoro-1,3-benzodioxol-4-yl)pyrrole-3-carbonitrile (SYN549129) (max. 1 g/kg) of ecotoxicological relevance
Molecular formula	$C_{12}H_6F_2N_2O_2$
Molecular mass	248.2 g/mol
Structural formula	

Physical and chemical properties

Melting point (state purity)	199.8°C (purity 99.8%)
Boiling point (state purity)	Not determined since thermal decomposition starts at about 306°C
Thermal stability / Temperature of decomposition	Thermal decomposition starts at about 306°C

Appearance (state purity)	Powder, Light olive green, Odourless (purity 96.8%) Fine powder, Faintly yellow, Odourless (purity 99.9%)
Relative density (state purity)	Bulk density = 1.54 x 10^3 kg/m^3 corresponding to a relative density of 1.54 (purity 99.8%)
Surface tension (state temperature and concentration of the test solution)	47.7 - 48.5 mN/m (Concentration 1.8 mg/L, 100% saturated solution, Temperature: 20ºC)
Vapour pressure (in Pa, state temperature)	3.9 x 10^{-7} Pa (extrapolated) (Temperature: 25ºC)
Henry's law constant (Pa m^3 mol^{-1})	5.4 x 10^{-5} Pa m³/mol (Calculated at 25 ºC)
Solubility in water (g/l or mg/l, state temperature)	1.8 mg/l (covers pH range 5 to 9 due to no dissociation in this interval, independent of temperature)
Solubility in organic solvents (in g/l or mg/l, state temperature)	Temperature: 25ºC Acetone: 190 g/l Dichloromethane: 7.3 g/l Ethyl acetate: 86 g/l Hexane: 10 mg/l Methanol: 42 g/l Octanol: 20 g/l Toluene: 2.7 g/l
Stability in organic solvents used in biocidal products including relevant breakdown products	Not applicable
Partition coefficient (log P_{OW}) (state temperature)	log Pow = 4.12 (covers pH range 5 to 9 due to no dissociation in this interval, Temperature: 25ºC)
Dissociation constant	The estimated dissociation constants of fludioxonil in water were found to be: pK_{a1} < 0 (basic) pK_{a2} ~14.1 (acidic)
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	The molar extinction coefficient [l/mol · cm] were determined to be: Neutral solution: 12384 (λ_{max} = 266 nm) Acidic solution: 12327 (λ_{max} = 265 nm) Basic solution: 11790 (λ_{max} = 271 nm) No absorption maximum between 340 and 750 nm
Flammability or flash point	Not a flammable solid
Explosive properties	Not an explosive

Oxidising properties	Not an oxidising solid
Auto-ignition or relative self ignition temperature	Not a self heating substance

Classification and proposed labelling

with regard to physical hazards	-
with regard to human health hazards	-
with regard to environmental hazards	H410

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	The determination of the active substance, fludioxonil, was carried out using high performance liquid chromatography on a reversed phase C18 column using a linear gradient program and UV detection at 270 nm. Quantification was achieved by comparison of peak area with an external standard.
Impurities in technical active substance (principle of method)	The analytical method for the determination of impurities in the active substance as manufactured is confidential. This information is provided separately in the confidential part of the dossier.

Analytical methods for residues

Soil (principle of method and LOQ)	LC-MS/MS (2 transitions, m/z 247 to 180 (primary) and m/z 247 to 126 (confirmatory)); LOQ: 0.01 mg/kg
Air (principle of method and LOQ)	HPLC-UV RP (268 nm), LOQ: 2 µg/m^3
Water (principle of method and LOQ)	LC-MS/MS (2 transitions, m/z 246.9 to 179.9 (primary), m/z 246.9 to 125.9 (confirmatory); LOQ for fludioxonil in river water, ground water and surface water: 0.05 µg/L
Body fluids and tissues (principle of method and LOQ)	Fludioxonil is not classified as toxic or highly toxic. Therefore, methods for the determination of residues in animal and human body fluids and tissues are not required.

Food/feed of plant or animal origin (principle of method and LOQ for methods for monitoring purposes)	For the specified uses under PT7, PT9 and PT10, fludioxonil and the formulated product Sporgard WB are not used for the treatment of food or feedingstuffs, or for the treatment of surfaces coming into contact with food or feeding stuffs. Therefore, methods for the determination of residues in food and feedingstuffs are not required.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	>80 % (based on urinary (13-20%) and biliary (68%) excretion within 24 h) rat study with bile cannulated animals
Rate and extent of dermal absorption*:	Dilution (0.05% fludioxonil)= 3 % (6 hr) A dermal absorption of 3% for both the concentrate and in use concentrations has been used in the risk assessment for the representative product. (*In vitro* dermal absorption of fludioxonil through human epidermis. Fludioxonil 230 g/l SC formulation ([redacted])).
Distribution:	Uniformly distributed (highest residues found in liver & kidney)
Potential for accumulation:	No evidence for accumulation
Rate and extent of excretion:	Rapid and extensive (>90 %) within 48 h, mainly via faeces (78-83%) and urine (13-20 %) within 24 h. The excretion was mainly bile.
Toxicologically significant metabolite(s)	-

* the dermal absorption value is applicable for the active substance and might not be usable in product authorization

Acute toxicity

Rat LD_{50} oral	> 5000 mg/kg bw
Rat LD_{50} dermal	> 2000 mg/kg bw
Rat LC_{50} inhalation	> 2.6 mg/L air /4h (nose only)

Skin corrosion/irritation	Non-irritant

Eye irritation	Non-irritant

Respiratory tract irritation	-
Skin sensitisation (test method used and result)	Non-sensitiser (M&K test and supporting data)
Respiratory sensitisation (test method used and result)	-

Repeated dose toxicity

Short term

Species / target / critical effect	Rat (oral): Effects on liver and kidney Rat (dermal): phagocytic cells in thymus in females
Relevant oral NOAEL / LOAEL	100 mg/kg bw day (28 day rat study)
Relevant dermal NOAEL / LOAEL	200 mg/kg bw day, females 1000 mg/kg bw day, males (highest dose) (3 weeks dermal rat study)
Relevant inhalation NOAEL / LOAEL	-

Subchronic

Species/ target / critical effect	Rat; liver (increased weight, hepatocyte hyperthrophy and kidney (increased relative weight and chronic nephropathy. Dog; liver (decreased bw and increased a/r liver weight, histopathological changes), bile duct proliferation & mild anemia in females.
Relevant oral NOAEL / LOAEL	58.5 mg/kg bw day (90-day dog) 64 mg/kg bw day (90-day rat) 33 mg/kg bw day (1 year dog study)[13]
Relevant dermal NOAEL / LOAEL	No studies submitted, not required.
Relevant inhalation NOAEL / LOAEL	No studies submitted, not required.

Long term

Species/ target / critical effect	Rat: Liver (gross and histopathological findings) Kidney (nephropathy males only) and blood (signs of mild anemia females)
Relevant oral NOAEL / LOAEL	NOAEL 37 mg/kg bw day (2 year; rat)
Relevant dermal NOAEL / LOAEL	No studies submitted, not required.

[13] Differences in NOAELs are due to the dose setting regime; LOAELs are similar in the two dog studies.

Relevant inhalation NOAEL / LOAEL	No studies submitted, not required.

Genotoxicity

	Based on the weight of evidence fludioxonil is unlikely to be genotoxic

Carcinogenicity

Species/type of tumour	Fludioxonil is unlikely to pose a risk to humans.
Relevant NOAEL/LOAEL	-

Reproductive toxicity

Developmental toxicity

Species/ Developmental target / critical effect	Maternal: reduced bw gain Foetuses: no effects
Relevant maternal NOAEL	100 mg/kg bw day (rabbit) 100 mg/kg bw day (rat)
Relevant developmental NOAEL	300 mg/kg bw day (rabbit) 1000 mg/kg bw day (rat)

Fertility

Species/critical effect	Parental & offspring: reduced bw and bw gain. No reproductive effects.
Relevant parental NOAEL	21 mg/kg bw day
Relevant offspring NOAEL	21 mg/kg bw day
Relevant fertility NOAEL	212 mg/kg bw day

Neurotoxicity

Species/ target/critical effect	No studies submitted; no concern from other studies

Developmental Neurotoxicity

Species/ target/critical effect	No studies submitted; no concern from other studies

Immunotoxicity

Species/ target/critical effect	No studies submitted; no concern from other studies

Developmental Immunotoxicity

Species/ target/critical effect	No studies submitted; no concern from other studies

Other toxicological studies

No studies submitted.

Medical data

No adverse effects on health in manufacturing personnel. No cases of poisoning are reported. No epidemiological studies are available.

Summary

	Value	Study	Safety factor
$AEL_{long\text{-}term}$	**0.37 mg/kg bw day**	2 year oral rat study (no correction for oral absorption)	**100**
$AEL_{medium\text{-}term}$	**0.59 mg/kg bw day**	90 day oral dog study (no correction for oral absorption)	**100**
$AEL_{acute/short\text{-}term}$	**1mg/kg bw day**	28 day oral rat study (no correction for oral absorption)	**100**
ADI[14]	**0.37 mg/kg bw day** Not relevant for the applied use (PT7, PT9 and PT10)	2 year oral rat study	**100-**
ARfD	Not allocated-not necessary	**-**	**-**

MRLs

Relevant commodities	Not relevant; exposure to feed or food not anticipated.

Reference value for groundwater

According to BPR Annex VI, point 68	0.1 µg/L (Directive 98/83/EC)

Dermal absorption

[14] If residues in food or feed.

Study (*in vitro/vivo*), species tested	*In vitro* dermal absorption of fludioxonil through human epidermis. Fludioxonil 230 g/L SC formulation ([redacted]).
Formulation (formulation type and including concentration(s) tested, vehicle)	SC formulation (0.05% and 23.3 % fludioxonil tested)
Dermal absorption values used in risk assessment	3% for both in use concentration and concentrate.

Acceptable exposure scenarios (including method of calculation)

Formulation of biocidal product	Sporgard WB contains about 2% w/w fludioxonil (about 20 g fludioxonil/L). Sporgard WB is an aqueous dispersion and the type of formulation can be described as a suspension concentrate (SC).
Intended uses	Fludioxonil is a fungicide that is used in the material preservative product Sporgard WB. Fludioxonil itself is only handled by industrial users who manufacture the representative biocidal product, Sporgard WB, and incorporate it into preserved end-use products. Fludioxonil is not used directly by professional users or the general public. End-use products preserved using Sporgard WB are sold for use by professional users and the general public (i.e. consumers). <u>PT7: Film preservatives</u> Sporgard WB is intended to be used as a film preservative in end-use products such as water-based paints and coatings and mineral sealants and fillers. <u>PT9: Preservatives for paper</u> Sporgard WB is intended to be used to treat paper which is used to produce drywall in order to prevent fungal growth. <u>PT10: Masonry preservatives</u> Sporgard WB is used to treat gypsum plaster used in drywalls (e.g. plasterboard, wallboard or gypsum board) in order to prevent fungal growth.

Industrial users	Acceptable uses were identified in the risk characterization of systemic effects (without PPE) for industrial workers in PT7, PT9 and PT11 *(RISKODERM Loading liquid, automated or semi-automated).* Acceptable use was identified in in the risk characterization of systemic for PT7 (PPE:gloves) for industrial workers conducting maintenance work of machines effects *(ECHA biocides Guidance 2015:dermal algorithm).* *(For details of calculations and %AEL please refer to section 8 &12 for the different scenarios.)*
Professional users	Acceptable uses were identified (without PPE) in the risk characterization of systemic effects for professionals workers in PT7 and PT10 in all reasonable scenarios. No direct professional uses was anticipated for this PT9 use (drywall coating paper). *(For details of calculations and %AEL please refer to section 8 &12 for the different scenarios.)*
Non professional users	Acceptable uses were identified (without PPE) in the risk characterization of systemic effects for non-professionals users for PT7 and PT10 in all reasonable scenarios. *(For details of calculations and %AEL please refer to section 8 &12 for the different scenarios.)*
General public	Secondary exposure levels were generally low and acceptable for the calculated scenarios. *(For details of calculations and %AEL please refer to section 8 &12 for the different scenarios.)*
Exposure via residue in food	Not relevant.

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)	pH 5: stable after 30 days (25 °C)
pH 7	pH 7: stable after 30 days (25 °C)
pH 9	pH 9: stable after 30 days (25 °C)

Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Latitude 30°N: DT50 = 9.9 days (25 °C) Latitude 40°N: DT50 = 8.7 days (25 °C) Highest DT50 = 9.9 days at 25 °C (28 days converted to 12 °C) Major photo-degradation products: GCA 339833 (max. 30.5% AR), CGA 344623 (max. 12.4% AR) and A5 (11.5% AR)
Readily biodegradable (yes/no)	Not readily biodegradable
Inherent biodegradable (yes/no)	No study
Biodegradation in freshwater	No study
Biodegradation in seawater	No study
Non-extractable residues	No data
Degradation in water / sediment systems (active substance)	<u>Whole system (degradation)</u> DT50 (20 °C) - Pond (near Tugbach, CH): 699 days - River (Rhine): 451 days DT50 (converted to 12 °C) - Pond (near Tugbach, CH): 1326 days - River (Rhine): 855 days Highest value used in risk assessment: 1326 days (12 °C)
Distribution in water / sediment systems (metabolites)	Formation of five minor metabolites (6.3%) was observed, but not identified further. Mineralisation to CO_2 accounted for less than 2% AR

Route and rate of degradation in soil

Mineralization (aerobic)	Fludioxonil was slightly degradable in soil, with CO_2 formation of 0.6 - 11.1% AR (pyrrole labelled) and 10.8 - 20.5% AR (phenyl-labelled) after 90 days at 20 ºC
Laboratory studies (range or median, with number of measurements, with regression coefficient)	
DT_{50lab} (20°C, aerobic):	<u>Aerobic biodegradation:</u> <u>Fludioxonil:</u> DT50 range from 143 to 482 days (geo. Mean of 265 days, n = 8, 20 °C), 502 days at 12 °C recalculated by Arrhenius equation. <u>CGA 192155:</u> DT50 range from 16 to 24 days (highest value of 24 days, n = 3, 20 °C), 46 days at 12 °C recalculated by Arrhenius equation. <u>CGA 339833:</u> DT50 range from 9.3 to 16 days (highest value of 16 days, n = 3, 20 °C), 30 days at 12 °C recalculated by Arrhenius equation.

DT_{90lab} (20°C, aerobic):	Not calculated
DT_{50lab} (10°C, aerobic):	No data
DT_{50lab} (20°C, anaerobic):	> 1 year
degradation in the saturated zone:	
Field studies (state location, range or median with number of measurements)	No field studies
DT_{50f}:	No data
DT_{90f}:	No data
Anaerobic degradation	No anaerobic field study
Soil photolysis	<u>DT50 (Somersham sandy loam, 25 °C)</u> [pyrrole-14C]-fludioxonil: 10 days [phenyl-14C]-fludioxonil: 9 days <u>DT50 (Somersham sandy loam, converted to 12 °C)</u> [pyrrole-14C]-fludioxonil: 28 days [phenyl-14C]-fludioxonil: 25 days Highest DT50 = 10 days at 25 °C (28 days at 12 °C)
Non-extractable residues	<u>Aerobic biodegradation:</u> Bound residues of 2.4 – 18.0% AR (pyrrole labelled) and 17.3 – 19.4% AR (phenyl-labelled) after 90 days at 20 ºC
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	<u>Soil photolysis study (maximum levels)</u> [pyrrole-14C]-fludioxonil: 11.7% CGA 192155, 9.1% CGA 339833 and 12.3% CGA 265378 [phenyl-14C]-fludioxonil: 10% CGA 192155, 6% CGA 339833 and 2% CGA 265378
Soil accumulation and plateau concentration	No study

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	Ka: 14,000 L/kg (arithmetic mean, n=5, range 290-61,000 L/kg) Kd: 2,100 L/kg (arithmetic mean, n=4, range 650-3,500 L/kg) Kaoc: 145,600 L/kg (arithmetic mean, n=5, range 12,000-385,000 L/kg) Kdoc: 89,000 L/kg (arithmetic mean, n=4, range 27,000-195,000 L/kg) No pH dependency

Fate and behaviour in air

Direct photolysis in air	No study
Quantum yield of direct photolysis	No study
Photo-oxidative degradation in air	Tropospheric half-life: 6.7 hours (according to Atkinson, reaction with OH radicals, 24 hour day, 5 x 10^5 OH radicals/cm^3)
Volatilization	Slightly volatile from water (Henry's law constant of 5.4 x 10^{-5} m^3Pa/mol)

Reference value for groundwater

According to BPR Annex VI, point 68	Limit value of 0.1 µg/L

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

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Rainbow trout (*Oncorhynchus mykiss*)	96 h, flow-through	LC_{50}	0.23 mg/L (m)
Fathead minnow (*Pimephales promelas*)	28 d, early life stage, flow-through	NOEC	0.039 mg/L (m)
Invertebrates			
Daphnids (*Daphnia magna*)	48 h, flow-through	LC_{50}	0.40 mg/L (m)
Daphnids (*Daphnia magna*)	21 d, flow-through	NOEC	0.019 mg/L (m)
Algae			

Green algae (*Selenastrum capricornutum*)	48 h	ErC50 NOEC	0.21 mg/L (m) 0.027 mg/L (m)
Microorganisms			
Activated sludge from sewage treatment plant	3 h, static	EC50	> 102 mg/L (n), solubility was exceeded, therefore NOEC is set to 1.8 mg/L (solubility in water)
Sediment-dwelling organisms			
Chironomus riparius	28 d, static, spiked sediment	NOEC	40 mg/kg dry sediment (n)

Effects on earthworms or other soil non-target organisms

Acute toxicity to earthworm (*Eisenia foetida*)	14 d: LC_{50} > 1000 mg/kg dry soil (n) *(no conversion to the TGD standard organic matter content of 3.4%)*
Reproductive toxicity to earthworm (*Eisenia foetida*)	56 d: NOEC = 20 mg/kg dry soil (n) *(no conversion to the TGD standard organic matter content of 3.4%)*

Effects on plants

Acute toxicity to plants	Triricum aestivum, Lactuca sativa, Raphanus sativus OECD 208 with a product containing 2.61% fludioxonil (18 days) L/EC_{50} (emergence and growth) > 0.467 mg/kg dry soil (n) L/EC_{0} (emergence and growth) = 0.467 mg/kg dry soil (n) *(after conversion to the TGD standard organic matter content of 3.4%)*

Effects on soil micro-organisms

Nitrogen mineralization	EC_{50} > 3.69 mg/kg dry soil (n) (*after conversion to the TGD standard organic matter content of 3.4%)*
Carbon mineralization	EC_{50} > 3.69 mg/kg dry soil (n) *(after conversion to the TGD standard organic matter content of 3.4%)*

Effects on terrestrial vertebrates

Acute toxicity to mammals	Refer to mammalian data
Acute toxicity to birds	No data
Dietary toxicity to birds	No data
Reproductive toxicity to birds	No data

Effects on honeybees

Acute oral toxicity	No data
Acute contact toxicity	No data

Effects on other beneficial arthropods

Acute oral toxicity	No data
Acute contact toxicity	No data
Acute toxicity to ……..	No data

Bioconcentration

Bioconcentration factor (BCF)	BCF_{fish} measured = 366 L/kg wet fish (whole fish, steady state) The $BCF_{earthworm}$ is estimated according to the TGD to 159 L/kg wet earthworm
Depuration time (DT_{50})	< 2 days for fish
Depuration time (DT_{90})	no data
Level of metabolites (%) in organisms accounting for > 10 % of residues	Fish test: 10.7% of M2 (not identified further)

Chapter 6: Other End Points

None

Appendix IIa and IIb: Human exposure calculations

A) Please refer to the confidential Appendix VI for Appendix IIA (human exposure calculation).

B) Position paper regarding HCD data ([redacted]).

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

ppm	Incidence of lymphoma									
	0 (1st)	0 (2nd)	3	10	30	100	1000	3000	5000	7000
Females										
un. deaths 0-12 m	3/7	1/4	0/4	0/4	0/4	0/0	0/4	3/6	0/7	2/9
12 m sacrifice	0/7	0/9	1/9	0/9	2/9	0/10	2/10	0/8	0/5	1/9
un. deaths 13-18 m	1/6	3/12	2/6	0/7	4/10	2/4	4/9	3/9	0/14	2/31
18 m sacrifice	7/40	7/35	4/41	10/40	6/37	11/46	6/37	12/37	11/34	3/11
total	11/60	11/60	7/60	10/60	12/60	13/60	12/60	18/60	11/60	8/60
Incidence [%]	18	18	12	17	20	22	20	30	18	13
Males										
un. deaths 0-12 m	0/3	0/1	0/5	0/2	1/8	1/3	1/3	0/0	1/3	0/9
12 m sacrifice	0/9	0/10	0/8	0/10	0/7	0/9	0/10	0/10	1/10	0/9
un. deaths 13-18 m	0/5	2/12	0/9	1/11	1/13	1/6	2/10	2/11	1/10	0/28
18 m sacrifice	2/43	1/37	1/38	0/37	0/32	0/42	4/37	0/39	1/37	0/14
total	2/60	3/60	1/60	1/60	2/60	2/60	7/60	2/60	4/60	0/60

Historical controls: incidence of thymus hyperplasia and malignant lymphoma[#] in female CD-1 mice

Studies	A	B	C	D	E	F	Total	% (min-max)
Thymus hyperpl.	8	6	6	13	12	-		
Malign. lymphoma	4	2	4	3	4	11		
combined	12/50	8/60	10/60	16/50	16/50	11/60	73/330	**22 (13-32)**
%	24	13	17	32	32	18		

[#] The incidence of malignant lymphoma and thymus hyperplasia were combined as thymus hyperplasia is often indistinguishable from thymus lymphoma.

un. = unscheduled, m = months, hyperpl. = hyperplasia, malign. = malignant

Appendix 10.16 Historical Control Data - Lymphoma in Female CD-1 Mice

Environmental Health Center

Study	Week	Finding	Incidence	Combined*	%
A	78	Thymus Hyperplasia Malignant Lymphoma	8 4	12/50	24
B	78	Thymus Hyperplasia Malignant Lymphoma	6 2	8/60	13.3
C	78	Thymus Hyperplasia Malignant Lymphoma	6 4	10/60	16.7
D	78	Thymus Hyperplasia Malignant Lymphoma	13 3	16/50	32
E	78	Thymus Hyperplasia Malignant Lymphoma	12 4	16/50	32
F	78	Malignant Lymphoma	11	11/60	18.3

* The incidences of malignant lymphoma and thymus hyperplasia were combined for consideration as thymus hyperplasia often is indistinguishable from thymus lymphoma.

[redacted]

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F-00018: 2-YEAR CHRONIC TOXICITY/ONCOGENICITY STUDY WITH CGA-173506 IN RATS

TABLE 10.15.9 HEPATOCELLULAR TUMOR INCIDENCES IN HISTORICAL CONTROL STUDIES (CONT'D.)

HISTORICAL CONTROL LIVER TUMOR INCIDENCE IN INDIVIDUAL EHC STUDIES

MALES

STUDY	ADENOMA	CARCINOMA	ADENOMA + CARCINOMA
A	1/60 (1.7%)	0/60 (0%)	1/60 (1.7%)
B	3/60 (5%)	0/60 (0%)	3/60 (5%)
C	0/60 (0%)	3/60 (5%)	3/60 (5%)
D	8/60 (13.3%)	1/60 (1.7%)	9/60 (15%)
E	1/70 (1.4%)	0/70 (0%)	1/70 (1.4%)
F	0/70 (0%)	1/70 (1.5%)	1/70 (1.4%)
G	2/60 (3.3%)	0/60 (0%)	2/60 (3.3%)

FEMALES

STUDY	ADENOMA	CARCINOMA	ADENOMA + CARCINOMA
A	3/60 (5%)	1/60 (1.7%)	4/60 (6.7%)
B	6/60 (10%)	0/60 (0%)	6/60 (10%)
C	0/60 (0%)	0/60 (0%)	0/60 (0%)
D	2/60 (3.3%)	0/60 (0%)	2/60 (3.3%)
E	0/70 (0%)	1/70 (1.4%)	1/70 (1.4%)
F	1/70 (1.4%)	0/70 (0%)	1/70 (1.4%)
G	1/60 (1.7%)	0/60 (0%)	1/60 (1.7%)

[redacted]

Appendix III: Environmental emission (and exposure) calculations

Find the *confidential* Appendix III in the confidential Appendix VI.

Appendix IV: List of terms and abbreviations

The abbreviations listed in the following were used in addition to standard terms and abbreviations as described in the link below

http://echa.europa.eu/documents/10162/15623299/biocides_guidance_human_health_ra_iii_partb_en.pdf

Abbreviation	Explanation
DIY	Do-It-Yourself

Appendix V: Overall reference list

ACTIVE SUBSTANCE

IUCLID Section No	Author(s)	Year	Title Source Report No GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
Section 3	**Heading**				
3.1-01	Rodler, M.	1992	Report on general physico-chemical properties (technical grade active ingredient) Ciba-Geigy Münchwilen AG, Münchwilen, Switzerland Report No. EA-175120, 15.10.1992 GLP / Unpublished	Y	[redacted]
3.1-02	Das, R.	1998	Report on general physico-chemical properties (pure active ingredient) Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland Report No. 62940, 27.05.1998 GLP / Unpublished	Y	[redacted]
3.2-01	Rodler, M.	1992	Report on melting point/melting range Ciba-Geigy Münchwilen AG, Münchwilen, Switzerland Report No. EA-169432, GLP / Unpublished	Y	[redacted]
3.4-01	Das, R.	2000	Boiling point / boiling range of CGA 173506 Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland Report No. 80806, 03.03.2000 GLP / Unpublished	Y	[redacted]
3.5-01	Füldner, H.	1992	Report on density of solids Ciba-Geigy Ltd., Basel, Switzerland Report No. PP-92/11P.DES, 02.07.1992 GLP / Unpublished	Y	[redacted]
3.6-01	Stulz, J.	1998	Report on spectra Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland Report No. 63115, 23.07.1998 GLP / Unpublished	Y	[redacted]
3.7.1-01	Rordorf, B.	1992	Report on vapour pressure curve Ciba -Geigy Ltd., Basel, Switzerland Report No. PP-92-11P-VPC, 23.09.1992 GLP / Unpublished	Y	[redacted]

IUCLID Section No	Author(s)	Year	Title Source Report No GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
3.7.2-01	Burkhard, N.	1994	Henry`s law constant Syngenta Crop Protection AG, Basel, Switzerland Data Sheet, 24.07.1994 Non GLP / Unpublished	Y	[redacted]
3.8-01	Ryser, M.	1992	Report on surface tension of aqueous solutions Ciba-Geigy Ltd., Basel, Switzerland Report No. PP-92/23T.SUR, 06.10.1992 GLP / Unpublished	Y	[redacted]
3.9-01	Rodler, M.	1992	Report on water solubility Ciba-Geigy Münchwilen AG, Münchwilen, Switzerland Report No. EA-169432, 17.07.1992 GLP / Unpublished	Y	[redacted]
3.10-01	Rodler, M.	1992	Report on octanol / water partition coefficient Ciba-Geigy Münchwilen AG, Münchwilen, Switzerland Report No. EA-169432, 23.07.1992 GLP / Unpublished	Y	[redacted]
3.11-01	Schürch, H.	1992	Report on thermal stability and stability in air Ciba-Geigy Ltd., Basel, Switzerland Report No. PP-92/23T.TSA, 07.09.1992 GLP / Unpublished	Y	[redacted]
3.11-02	Das, R.	2000	Boiling point / boiling range of CGA 173506 Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland Report No. 80806, 03.03.2000 GLP / Unpublished	Y	[redacted]
3.12-01	Kettner, R.	2005	Final report on storage stability Ciba-Geigy AG, Switzerland Study No. 19065 GLP / Unpublished	Y	[redacted]
3.13-01	Jäkel,K.	1992	Report on dissociation constant in water Ciba-Geigy Ltd., Basel, Switzerland Report No. PP-92-11P-DCW, 27.07.1992 GLP / Unpublished	Y	[redacted]
3.14-01	Das, R.	2009	Fludioxonil Particle Size Distribution Syngenta Crop protection, Münchwilen AG, Münchwilen, Switzerland Study No. 120336, 16.09.2009 GLP / Unpublished	Y	[redacted]

IUCLID Section No	Author(s)	Year	Title Source Report No GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
3.16-01	Kettner ,R.	2000	Solubility in organic solvents of CGA 173506 Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland Report No. 80807, 16.02.2000 GLP / Unpublished	Y	[redacted]
Section 4	**Heading**				
4.1-01	Schürch, H.	1992	Report on explosive properties Ciba-Geigy Ltd., Basel, Switzerland Report No. PP-92/23T.EXP, 07.09.1992 GLP / Unpublished	Y	[redacted]
4.2-01	Schürch, H.	1992	Report on flammability of solids Ciba-Geigy Ltd., Basel, Switzerland Report No. PP-92/23T.FLS, 07.09.1992 GLP / Unpublished	Y	[redacted]
4.2-02	Jackson, W.A.	2004	Flammability (solids) – CGA173506 tech Syngenta Crop Protection, Switzerland Report No. HT04/365 GLP / Unpublished	Y	[redacted]
4.4-01	Schürch, H.	1992	Report on oxidizing properties Ciba-Geigy Ltd., Basel, Switzerland Report No. PP-92/23T.OXP, 07.09.1992 GLP / Unpublished	Y	[redacted]
4.17.1-02	Schürch, H.	1992	Report on auto-flammability of solids Ciba-Geigy Ltd., Basel, Switzerland Report No. PP-92/23T.AFS, 07.09.1992 GLP / Unpublished	Y	[redacted]
Section 5	**Heading**				
5-01	Kettner ,R.	2005	CGA173506 tech. Analysis of five representative batches producted at Monthey Syngenta Crop Protection, Switzerland Report No. 115094, 06.09.2005 GLP / Unpublished	Y	[redacted]
5-02	Das, R.	2011	Analysis of five representative batches produced by Fine Organics Limited Syngenta Crop Protection, Switzerland Report No. 122948, 09.05.2011 GLP / Unpublished	Y	[redacted]

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5-03	Kettner ,R.	2016	[redacted]	Y	[redacted]
5-04	Duell B.	2016	[redacted]	Y	[redacted]
5-05	Mink C.	2016	[redacted]	Y	[redacted]
5.1-01, 5.1-02	Tomann, A.	1992	Analytical method for CGA 173506, Ciba-Geigy Ltd., Basel, Switzerland, Report number AW-156-4, Non-GLP / Unpublished.	Y	[redacted]
5.1-01, 5.1-02	Tomann, A.	1992	Method validation for technical active substance – AW156-4, Ciba-Geigy Ltd., Basel, Switzerland, Report number not stated, Non GLP / Unpublished.	Y	[redacted]

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5.1-03, 5.1-04	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5.1-03, 5.1-04	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5.1-05	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5.1-06	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5.1-07	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

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5.2.1-01	Robinson, N.J. and Tummon, O.J	2004	Residue analytical method for the determination of fludioxonil in soil, Syngenta, Bracknell, UK., Report number RAM 423/01, GLP / Unpublished.	Y	[redacted]
5.2.1-02	Braid, S.	2015	Fludioxonil - Analytical Method GRM025.06A for the Determination of Fludioxonil in Soil.	Y	[redacted]
5.2.1-02	Hamberger, R.	2015	Fludioxonil – Validation of Analytical Method GRM025.06A for the Determination of Fludioxonil (CGA173506) in Soil	Y	[redacted]
5.2.1-03	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5.2.1-03	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5.2.2-01	Tribolet, R.	1992	Sampling of air and determination of residues of parent compound by high performance liquid chromatography. Syngenta Crop Protection AG, Basel, Switzerland, Report number 115/92, GLP / Unpublished.	Y	[redacted]
5.2.2-02	Tribolet, R.	1996	Validation of method REM 133.03 in air – Validation by analysis of fortified specimens and determination of recoveries, Ciba-Geigy Ltd., Basel, Switzerland, Report number 103/96, GLP / Unpublished.	Y	[redacted]

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5.2.2-03	Tribolet, R.	2001	Appendix No. 1 to sampling of air and determination of residues of parent compound by high performance liquid chromatography – confirmatory technique, Syngenta Crop Protection AG, Basel, Switzerland, Report number 115/92, GLP / Unpublished.	Y	[redacted]
5.2.3-01, 5.2.3-02	Robinson, N.J.	2007	Fludioxonil: Residue analytical method for the determination of residues of fludioxonil and its metabolites CGA192155 and CGA339833 in water, Syngenta, Bracknell, UK, Report number GRM025.01A, GLP / Unpublished.	Y	[redacted]
5.2.3-01, 5.2.3-02	Nagra, B.S.	2007	Validation of a residue analytical method (GRM025.01A) for the determination of residues of fludioxonil and its metabolites CGA192155 and CGA339833 in water, Syngenta, Bracknell, UK, Report number T003490-06-REG, GLP / Unpublished.	Y	[redacted]

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Section 6	**No references submitted**				
6.6-01	Gerharz, T.	2014	Determination of the antimicrobial effects of Sporgard WB and Fludioxonil against fungi, LANXESSS Deutschland GmbH, Leverkusen, Germany, Report No. M 2012-32-3, M2011-63 Non-GLP / Unpublished.	Y	[redacted]
6.6-01	Rech		Method: Determination of the Minimal Inhibitory Concentration (MIC) of test substances against bacteria and fungi LANXESSS Deutschland GmbH, Leverkusen, Germany, Method No. M 2 02-00012-12E Non-GLP / Unpublished.	Y	[redacted]
6.6-02	Knauf-Beiter, G; Gerber, T; Theiler, M	2005	Syngenta active ingredients for use in Material Protection Reserach Biology, Disease Control (Stein) RT 4.33 Report No. 08F report 2005004 Non-GLP / Unpublished.	Y	[redacted]
6.6-02	-	2009	Data Sheet A7850C WP (50) Fludioxonil	Y	[redacted]
6.6-02	-	2005	Data Sheet A-9859 A SC (230) Fludioxonil	Y	[redacted]
Section 7	**No references submitted**				
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8.1-01	[redacted]	1988	CGA 173506 tech. - Acute dermal irritation/corrosion study in the rabbit. [redacted] Report no: 881487, 08.08.1988 GLP / Unpublished	Y	[redacted]
8.1-02	[redacted]	1991	Primary dermal irritation study of CGA 173506 technical in rabbits. [redacted] Report no: HWI 10200146, 14.06.1991 GLP / Unpublished	Y	[redacted]

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8.2-01	[redacted]	1988	CGA 173506 tech. - Acute eye irritation/corrosion study in the rabbit [redacted] Report no: 881486, 12.08.1988 GLP / Unpublished	Y	[redacted]
8.3-01	[redacted]	1988	Skin sensitisation test in the Guinea pig with CGA 173506 tech. - Maximisation test. [redacted] Report no: 881490, 19.12.1988 GLP / Unpublished	Y	[redacted]
8.3-02	[redacted]	1999	CGA 173506 FS 025, (A-8207 I) - Skin sensitization in the Guinea pig (Maximization test) [redacted] 993014, 01.03.1999 [redacted] GLP / Unpublished	Y	[redacted]
8.5.1-01	Ogorek, B.	1989	Salmonella and Escherichia/liver-microsome test Ciba-Geigy Ltd., Genetic Toxicology, Basel, Switzerland. Report no: 881495, 02.02.1989 GLP / Unpublished	Y	[redacted]
8.5.1-02	Chang, S	2016	Fludioxonil tech. - Salmonella Typhimurium and Escherichia Coli Reverse Mutation Assay. Envigo Report No. 1770600 Envigo CRS GmbH, Germany. GLP / Unpublished	Y	[redacted]
8.5.1-03	Bowles, A	2009	Technical Fludioxonil – Reverse Mutation Assay "Ames Test" using Salmonella typhimurium and Escherichia coli. Harlan Laboratories Ltd. unpublished report no: 2364/0457, 17.04.2009 GLP	Y	[redacted]
8.5.2-01	Strasser, F.F.	1989	Chromosome studies on Chinese hamster ovary cell line CCl 61 *in vitro* (OECD conform). Ciba-Geigy Ltd., Genetic Toxicology, Basel, Switzerland. Report no: 881496, 07.11.1989 GLP / Unpublished	Y	[redacted]

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8.5.3-01	Dollenmeier, P.	1989	Point mutation test with Chinese hamster cells V79 (OECD conform). Ciba-Geigy Ltd., Genetic Toxicology, Basel, Switzerland. Report no: 881497, 03.02.1989 GLP / Unpublished	Y	[redacted]
8.6-01/1	[redacted]	1990	Micronucleus test, mouse [redacted] Report no: 881493, 03.01.1990 GLP / Unpublished	Y	[redacted]
8.6-01/2	[redacted]	2007	CGA278466 - Micronucleus Assay in Bone Marrow Cells of the Mouse [redacted] Report No. 1086800 GLP / Unpublished	Y	[redacted]
8.6-02	[redacted].	1993	Chromosome studies on somatic cells of Chinese hamster (OECD conform) – *in vivo* study. [redacted] Report no: 923099, 06.01.1993 GLP / Unpublished	Y	[redacted]
8.6-03	[redacted]	1993	*In vivo/in vitro* unscheduled and replicative DNA synthesis in rat hepatocytes. [redacted] Report no: 933031, 27.08.1993 GLP / Unpublished	Y	[redacted]
8.7.1-01	[redacted]	1991	Acute oral toxicity study of CGA 173506 technical in rats. [redacted] Report no: HWI 10200144, 25.04.1991 GLP / Unpublished	Y	[redacted]
8.7.2-01	[redacted]	1989	Acute inhalation toxicity in the rat - CGA 173506 tech. [redacted] Report no: 881491, 20.04.1989 GLP / Unpublished	Y	[redacted]
8.7.3-01	[redacted]	1988	Acute dermal toxicity in the rat with CGA 173506 technical. [redacted] Report no: 881489, 26.09.1988 GLP / Unpublished	Y	[redacted]

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8.8.1-01	[redacted]	1990	Fludioxonil: absorption, distribution, metabolism and excretion of [4-^{14}C]pyrrole CGA 173506 in the rat. [redacted] Report No. 32/90 (23RB01, 23RB02); 15.10.1990 GLP / Unpublished	Y	[redacted]
8.8.1-02	[redacted]	1992	Metabolic pathways of [4-^{14}C]pyrrole CGA 173506 in the rat. [redacted] Report No. 12/92 (05PT01); 02.11.1992 GLP / Unpublished	Y	[redacted]
8.8.1-03	[redacted]	1995	Fludioxonil: absorption and distribution kinetics of [4-^{14}C]pyrrole CGA 173506 in the rat after oral administration. [redacted] Report No. 4/95 (023AM01); 22.03.1995 GLP / Unpublished	Y	[redacted]
8.8.1-04	[redacted]	1994	On the nature and the extent of the urine coloration observed after subchronic and chronic administration of CGA 173506 to rats. [redacted] Report no: 13/93 (05PT02); 06.01.1994 GLP / Unpublished	Y	[redacted]

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8.8.2-01	[redacted]	1999	The *in vitro* percutaneous absorption of [Phenyl-U-^{14}C] CGA 173506 formulated as SWITCH® 62.5 WG (A-9219 B) through rat and human epidermis. [redacted] Report to study No. 023AM03, 08.12.1999 GLP / Unpublished	Y	[redacted]
8.8.2-02	[redacted]	1999	Dermal absorption of [Phenyl-U-^{14}C] CGA 173506 formulated as SWITCH® 62.5 WG (A-9219 B) in the rat. [redacted] Report no. 023AM02, 06.04.1999 GLP / Unpublished	Y	[redacted]
8.8.2-03	Davies D J	2005	Fludioxonil 230g/l SC formulation ([redacted]): *In vitro* dermal absorption of fludioxonil through human epidermis. Syngenta Limited, Alderley Park, UK Study No. T022392-04, 03.06.2005 GLP / Unpublished.	Y	[redacted]
8.8.2-04	Davies D J	2005	Fludioxonil/Cyprodinil 62.5 WG ([redacted]): In vitro dermal absorption of fludioxonil through rat epidermis. Central Toxicology Laboratory, Alderley Park, UK Study No. JV1872 Report No. CTL/JV1872/REGULATORY/REPORT GLP / Unpublished.	Y	[redacted]
8.8.2-05	Davies D J	2005	Fludioxonil/Cyprodinil 62.5 WG ([redacted]): In vitro dermal absorption of fludioxonil through human epidermis. Central Toxicology Laboratory, Alderley Park, UK Study No. JV1871 Report No. CTL/JV1871/REGULATORY/REPORT GLP / Unpublished.	Y	[redacted]

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8.9.1.1-01	[redacted].	1990	28-Day oral cumulative toxicity study in rats (gavage) - CGA 173506 tech. [redacted] Report no: 881492, 17.05.1990 GLP / Unpublished	Y	[redacted]
8.9.1.1-02	[redacted]	1990	CGA 173506: 90-Day oral toxicity study in rats. [redacted] Report no: F-00014; 16.01.1990 GLP / Unpublished	Y	[redacted]
8.9.1.1-03	[redacted]	1990	Toxicity study by repeated oral administration for 13 weeks followed by a 28-day recovery period in Beagle dogs - CGA 173506 tech. [redacted] Report no: 881173 (4279TCC), 21.05.1990 GLP / Unpublished	Y	[redacted]
8.9.1.1-05	[redacted]	1993	18-Month dietary oncogenicity study with CGA 173506 in mice. [redacted] Report no: F-00019, 26.01.1993 GLP / Unpublished	Y	[redacted]
8.9.1.1-06	[redacted]	1993	18-Month dietary oncogenicity study with CGA 173506 in mice. [redacted] Report no: F-00071, 27.01.1993 GLP / Unpublished	Y	[redacted]
8.9.1.1-07	[redacted]	1993	First addendum to the final report 2-Year chronic toxicity/oncogenicity study in rats. [redacted] Report no: F-00018, 30.01.1993 GLP / Unpublished	Y	[redacted]
	[redacted]	1994	Amendment 2 to final report '2-Year chronic toxicity/oncogenicity study in rats*(study report N° F-00018)' 17.11.1994 [redacted] GLP / Unpublished	Y	[redacted]

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8.9.1.1-08	[redacted]	1992	Toxicity study by repeated oral (dietary) administration for 52 weeks in Beagle dogs. [redacted] Study report N° 5577 TCC / CG 881174, 18.06.1992 [redacted] GLP / Unpublished	Y	[redacted]
8.9.1.3-01	[redacted]	1990	28-Day repeated dose dermal toxicity study in the rat - CGA 173506 tech. [redacted] Report no: 881488, 26.08.1990 GLP / Unpublished	Y	[redacted]
8.10.1-01	[redacted]	1989	Assessment of possible embryotoxic or teratogenic effects in rats by oral route. [redacted] Report no: 881177 (4517 RSR), 02.11.1988 GLP / Unpublished	Y	[redacted]
8.10.1-02	[redacted]	1989	Assessment of possible embryotoxic or teratogenic effects in rabbits by oral route. [redacted] Report no: 881728 (4801 RSL), 23.10.1989 GLP / Unpublished	Y	[redacted]
8.10.2-01	[redacted]	1992	A two-generation reproductive toxicity study in rats. [redacted] Report no: 902001, 21.05.1992 GLP / Unpublished	Y	[redacted]
8.12.1	[redacted]	2003	CGA 173506 – Fludioxonil Medical Data [redacted] Non-GLP, Unpublished	Y	[redacted]
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9.1.1-01	[redacted]	1993	A 96-hour flow through acute toxicity test with rainbow trout (*Oncorhynchus mykiss*). [redacted] GLP, Unpublished.	Y	[redacted]
9.1.1-02	[redacted]	1997	CGA-173506 technical – acute toxicity to rainbow trout, *Oncorhynchus mykiss*, under flow-through conditions. [redacted] Report no. 276-89. GLP, Unpublished.	Y	[redacted]
9.1.1-03	[redacted]	1997	CGA-173506 technical – acute toxicity to bluegill sunfish, *Lepomis macrochirus*, under flow-through conditions amended report. [redacted] Report no. 277-89. GLP, Unpublished.	Y	[redacted]
9.1.1-04	[redacted]	1993	A 96-hour flow through acute toxicity test with the sheepshead minnow (*cyprinodon variegates*). [redacted] Report no. 108A-135. GLP, Unpublished.	Y	[redacted]
9.1.2-01	Surprenant, D.C.	1990	CGA 173506 technical – acute toxicity to daphnids (*Daphnia magna*) under flow-through conditions Springborn Laboratories Inc., Report no. 89-05-2990. GLP, Unpublished.	Y	[redacted]
9.1.2-02	Holmes, C.M., Swigert, J.P.	1993	A 48-hour flow through acute toxicity test with the cladoceran (*Daphnia magna*) Wildlife International Ltd., Report no. 108A-133. GLP, Unpublished.	Y	[redacted]
9.1.3-01	Rufli, H.	1989	Algae, growth inhibition test of CGA 173506 technical to green algae (*Scenedesmus subspicatus*). Ciba Geigy Ltd., Report no. 881737. GLP, Unpublished.	Y	[redacted]
9.1.3-02	Hoberg, J.R.	1992	CGA 173506 techn. – toxicity to the freshwater algae (*Selenastrum capricornutum*). Springborn Laboratories Inc., Report no. 92-9-4399. GLP, Unpublished.	Y	[redacted]

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9.1.5-01	Weinstock, M.	1994	Report on the test for activated sludge respiration inhibition of CGA 173506 tech. Ciba-Geigy Basel, Report no. 943544. GLP, Unpublished.	Y	[redacted]
9.1.6.1-01	[redacted]	1993	Report on the prolonged toxicity test of CGA 173506 tech. to rainbow trout. [redacted] Report no. 938218. GLP, Unpublished.	Y	[redacted]
9.1.6.1-02	[redacted]	1993	Report on the prolonged toxicity test of CGA 173506 tech. to rainbow trout. [redacted] Report no. 938217. GLP, Unpublished.	Y	[redacted]
9.1.6.1-03	[redacted]	1993	Report on the prolonged toxicity test of CGA 173506 tech. to rainbow trout. [redacted]., Report no. 938033. GLP, Unpublished.	Y	[redacted]
9.1.6.1-04	[redacted]	2005	Fludioxonil (CGA 173506): determination of the effects on the growth rate of juvenile rainbow trout (*Oncorhynchus mykiss*) using a continuous flow system. [redacted] Report no. BL8185/B. GLP, Unpublished.	Y	[redacted]
9.1.6.1-05	[redacted]	1994	CGA 173506 – An early life stage toxicity test with the fathead minnow (*Pimephales promelas*) [redacted] Report no. 108A-153. GLP, Unpublished.	Y	[redacted]
9.1.6.2-01	Putt, A. E.	1991	(CGA 173506 technical) – Chronic toxicity to daphnids (*Daphnia magna*) under flow-through conditions. Springborn Laboratories Inc., Report no. 91-2-3672. GLP, Unpublished.	Y	[redacted]

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9.1.6.2-02	Rufli, H	1989	Daphnia reproduction test with CGA 173506 technical. Ciba-Giegy Ltd., Report no. 881736. GLP, Unpublished.	Y	[redacted]
9.1.6.2-03	Fournier, A.	2014	Fludioxonil – Full Life-Cycle Toxicity Test with Water Fleas, Daphnia magna, Under Static Renewal Conditions, Smithers Viscient Report Number 1781.6936 GLP, Unpublished.	Y	[redacted]
9.1.7-02	[redacted]	1994	Accumulation and elimination of ^{14}C-CGA 173506 by bluegill sunfish (*Lepomis macrochirus*) in a dynamic flow-through system [redacted] Report no. 93GJ02. GLP, Unpublished.	Y	[redacted]
9.1.8-01	Giddings, J. M	1993	CGA 173506 Outdoor aquatic microcosm study of the environmental fate and ecological effects. Springborn Laboratories Inc., Report no. 92-12-4548 GLP, Unpublished.	Y	[redacted]
9.1.9-01	Grade, R.	1998	Toxicity test of CGA 173506 tech. on sediment-dwelling *Chironomus riparius* (Syn. *Chironomus thummi*) under static conditions. Novartis Crop Protection AG, Report no. 983752. GLP, Unpublished.	Y	[redacted]
9.2.1-01	Schanné, C. & Galicia, H.	1992	The effect of CGA 173506 on soil respiration and nitrification. RCC AG, Report No.: 315843 GLP, Unpublished.	Y	[redacted]
9.2.1-02	Wüthrich, V.	1993	The effect of CGA 173506 on soil respiration and nitrification. RCC AG, Report No.: 344226 GLP, Unpublished.	Y	[redacted]
9.2.1-03	Grade, R.	2002	The effect of CGA 173506 tech on the growth of soil fungi on soil-malt extracts agar plates. Syngenta AG, Report No.: 2023529, GLP, Unpublished.	Y	[redacted]

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9.2.2-01	Rufli, H.	1989	Acute toxicity of CGA 173506 technical to Earthworm (*Eisenia foetida*). Ciba-Geigy Ltd., Report no. 881738. GLP, Unpublished.	Y	[redacted]
9.2.2-02	Friedrich, S.	2003	Fludioxonil (CGA 173506): Sublethal toxicity of the technical material to the earthworm Eisenia fetida. BioChem agrar, Report No.: 03 10 48 023 / 2023633, GLP, Unpublished.	Y	[redacted]
9.2.3-01	Porch, J.R & Krueger, H.O.	2002	A toxicity test to determine the effects of CGA 173065 025 FS (A-8207 I) on seedling emergence and growth of terrestrial plants. Wildlife International Ltd. Report No.: 528-136. GLP, Unpublished.	Y	[redacted]
9.2.3-02	Porch, J.R.; Martin, K.H.; Krueger, H.O.	2011	Fludioxonil - Toxicity effects on the seedling emergence of ten species of plants. Wildlife International Ltd. Report No.: 528-350. GLP, Unpublished.	Y	[redacted]
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10.1.1.1-01	Hawkins, D.R. Kirkpatrick, D. Shaw, D.	1991	The hydrolytic stability of CGA 173506 Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Report No. CBG-487-891775, GLP / Unpublished	Y	[redacted]
10.1.1.1-02	Van der Gaauw A.	2002	[U-Phenyl-^{14}C]-CGA 339833: Hydrolysis at Three Different pH Values; RCC Ltd., Environmental Chemistry, Zegliweg 1, Itingen, Switzerland; Report No. 812621 GLP / not published	Y	[redacted]
10.1.1.1-03	Kirkpatrick, D.	1994	The photodegradation of CGA 173506 in water (amended final report) Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Report No. CBG 488/9098, GLP / not published	Y	[redacted]

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10.1.1.1-04	Kirkpatrick, D.	1994	Photolysis of [Phenyl-U-^{14}C]CGA 173506 in aqueous solution under laboratory conditions Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Report No. CBG 609/942536, GLP / not published	Y	[redacted]
10.1.1.1-05/06	Kirkpatrick, D.	1994	The Photodegradation of [Pyrole-4-^{14}C]CGA 173506 on soil and in water: Identification of photoproducts Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Report No. CBG569/932273, GLP / not published	Y	[redacted]
10.1.1.1-05/06	Kirkpatrick, D.	1996	The photodegradation of CGA 173506 on soil and in water: co-chromatography of study samples with reference compounds Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Report No. CBG 720/951173, GLP / not published	Y	[redacted]
10.1.1.2-01	Baumann, W.	1993	Report on the test for ready biodegradability of CGA 173506 tech. in the carbon dioxide evolution test Ciba-Geigy Ltd, Basel, Switzerland Report No. 933653, GLP / not published	Y	[redacted]
10.1.2-01	Hawkins, D.R. Kirkpatrick, D. Shaw, D. Chan, S.C.	1991	Adsorption/desorption of CGA 173506 with soil Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Report No. CGA173506/0107, GLP / not published	Y	[redacted]
10.1.3-01	Gonzalez-Valero, J.	1992	Metabolism of CGA 173506 under aerobic conditions in aquatic systems Ciba-Geigy Ltd, Basel, Switzerland Report No. 21/92-91GJ03, GLP / not published	Y	[redacted]
10.2.1-01	Hawkins, D.R. Kirkpatrick, D. Shaw, D.	1991	The degradation of CGA 173506 in soil under aerobic, aerobic/anaerobic and sterile conditions at 25°C Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Report No. HRC-CBG-485-90818, GLP / not published	Y	[redacted]

IUCLID Section No	Author(s)	Year	Title Source Report No GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
10.2.1-02	Abildt, U.	1991	Rate of degradation of CGA 173506 in aerobic soil at various conditions Ciba-Geigy Ltd., Basel, Switzerland Report No. 1-91-90UA01, GLP / not published	Y	[redacted]
10.2.1-03	Ellgehausen	1992	Degradation of CGA-173506 in two soils under aerobic conditions at 20°C Ciba-Geigy Ltd., Basel, Switzerland Report No. 1/92-91EH05, GLP / not published	Y	[redacted]
10.2.1-04	Ellgehausen	1992	Degradation of CGA 173506 in one soil under aerobic conditions at two temperatures Ciba-Geigy Ltd., Basel, Switzerland Report No. 3/92-91EH08, GLP / not published	Y	[redacted]
10.2.1-05	Minet, U.	1994	Degradation and Metabolism of ^{14}C-Pyrrole-Labelled CGA 173506 in Soil under Aerobic and Aerobic/Anaerobic Conditions at 20°C Ciba-Geigy Ltd., Basel, Switzerland Report No. 14/93-92MU01-1, GLP / not published	Y	[redacted]
10.2.1-06	Minet, U.	1994	Degradation of ^{14}C-Pyrrole-Ring-Labelled CGA 173506 in Two Soils under Aerobic Conditions at 20°C Ciba-Geigy Ltd., Basel, Switzerland Report No. 15/93-92MU01-2, GLP / not published	Y	[redacted]
10.2.1-07	Minet, U.	1994	Degradation and Metabolism of Phenyl-Labelled CGA 173506 in Soil under Aerobic Conditions at 20°C Ciba-Geigy Ltd., Basel, Switzerland Report No. 4/94-92MU02, GLP / not published	Y	[redacted]
10.2.1-08	Reischmann, F.J.	1994	Degradation of CGA 173506 in Soil under controlled laboratory Conditions Ciba-Geigy Ltd., Basel, Switzerland Report No. 7/94-93RF02, GLP / not published	Y	[redacted]
10.2.1-09	Ulbrich, R.	1998	Rate of degradation of ^{14}C-Carbonyl labelled CGA 192155 in various soils at 20°C. Novartis Crop Protection AG, Basel, Report number 97UL04, GLP / not published	Y	[redacted]

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10.2.1-10	Ulbrich, R.	1999	Rate of degradation of Oxirane-3-^{14}C-labelled CGA 339833 in various soils at 20°C. Novartis Crop Protection AG, Basel Report number 98UL01, GLP / not published	Y	[redacted]
10.2.1-11	Adam, D.	1998	Anaerobic soil metabolism of ^{14}C-Phenyl-CGA 173506 in a sandy loam/water system Novartis Crop Protection AG, Basel, Switzerland Report No. 97DA01, GLP / not published	Y	[redacted]
10.2.1-14	Kirkpatrick, D.	1994	The photodegradation of CGA 173506 on soil (amended final report) Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Report No. HRC CBG 516/901362, GLP / not published	Y	[redacted]
10.2.1-15	Kirkpatrick, D.	1994	Photolysis of [Phenyl-U-^{14}C]CGA 173506 on the soil surface under laboratory conditions Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Report No. CBG 610/942382, GLP / not published	Y	[redacted]
10.2.1-16	Kirkpatrick, D.	1994	The Photodegradation of [Pyrrole-4-^{14}C]CGA 173506 on soil and in water: Identification of photoproducts Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Report No. CBG569A & CBG569B, GLP / not published	Y	[redacted]
10.3.1-01	Stamm, E.	1999	Atmospheric oxidation of fludioxonil CGA 173506 by hydroxyl radicals, Rate estimation Novartis Crop Protection AG, Basel, Switzerland Report No. 98SM19, Non-GLP / not published	Y	[redacted]

PRODUCT

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3.1-01, 3.2-01, 3.3-01	Irrig, H.	2007	A15996A- Color, Odor, Physical State, pH (1%), Viscosity and Density Syngenta Crop Protection Inc, Greensboro, NC USA 27409 Report No. PC-07-060 GLP/Unpublished	Yes	[redacted]
3.2-02	Wachtler, P	2014	pH-determination of Sporgard WB via pH-meter Report No. NA Lanxess Deutschland GmbH Non-GLP/Unpublished	Yes	[redacted]
3.4.1-03	Irrig, H	2008	One Year Storage Stability at Ambient Temperature and Corrosion Characteristics of Sporgard WB (A15996A) Syngenta Crop Protection Inc. Technology & Projects Report No. PC-08-041 GLP/Unpublished	Yes	[redacted]
3.4.1-04	Bickers, C	2014	2 Years Storage stability at ambient temperature of Sporgard WB Lanxess Deutschland GmbH Report No. NA Non GLP/ Unpublished	Yes	[redacted]
3.4.1-05	Irrig, H	2008	One Year Storage Stability at Ambient Temperature and Corrosion Characteristics of Sporgard WB (A15996A) Syngenta Crop Protection Inc. Technology & Projects Report No. PC-08-041 GLP/Unpublished	Yes	[redacted]
3.8-01	Keldenich, H.-P.	2014	Determination of Safety-Relevant Data of Sporgard WB Bayer Technology Services GmbH, D-51368 Leverkusen, Germany Report No. 2014/00072 GLP/Unpublished	Yes	[redacted]
3.9-01, 4.1-01, 4.2-01, 4.4-01	Irrig, H.	2007	Physical and Chemical Properties of Thiabendazole/Azoxystrobin/Fludioxonil 19.0/19.0/1.92 SC (A15996A) Syngenta Crop Protection Inc, Greensboro, NC USA 27409 Report No. PC-07-060 GLP/Unpublished	Yes	[redacted]

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3.9-02	Keldenich, H.-P.	2014	Determination of Safety-Relevant Data of Sporgard WB Bayer Technology Services GmbH, D-51368 Leverkusen, Germany Report No. 2014/00072 GLP/Unpublished	Yes	[redacted]
4.17.1-01	Keldenich, H.-P.	2014	Determination of Safety-Relevant Data of Sporgard WB Bayer Technology Services GmbH, D-51368 Leverkusen, Germany Report No. 2014/00072 GLP/Unpublished	Yes	[redacted]
5.1-01	Johnson, A.	2007	A15996A - Validation of Analytical Method SF-217/1 Syngenta Crop Protection, Inc Report No. 10238866 GLP/Unpublished	Yes	[redacted]
6.7-01	Twaddle, H.M.	2012	Mildew Resistance Report: Sporgard & Azotech Benchmark – Styrene Paint. Lanxess, Material Protection, Pittsburgh, USA. Report No. IR-1001 Non-GLP/Unpublished	Yes	[redacted]
6.7-02	Twaddle, H.M.	2012	Mildew Resistance Report: Sporgard & Azotech Benchmark – Vinyl Acrylic Paint. Lanxess, Material Protection, Pittsburgh, USA Report No. IR-1001 Non-GLP/Unpublished	Yes	[redacted]
6.7-03	Herbertz, T.	2012a	Efficacy of Sporgard WB as antifungal treatment of gypsum board Lanxess Deutschland GmbH, Leverkusen, Germany. Report No. Not specified Non-GLP/Unpublished	Yes	[redacted]
6.7-04	Herbertz, T.	2012b	Efficacy of Sporgard WB as antifungal treatment of paper Lanxess Deutschland GmbH, Leverkusen, Germany. Report No. Not specified Non-GLP/Unpublished	Yes	[redacted]
6.7-05	Herbertz, T.	2013	Efficacy of Sporgard WB in mineral sealant/grout. Lanxess Deutschland GmbH, Leverkusen, Germany Report No. Not specified Non-GLP/Unpublished	Yes	[redacted]

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6.7-06/07/08	Riethausen K	2009	Method: Determination of Minimum Inhibitory Concentration of Test Compounds, against Ascomycetes and Deuteromycete Lanxess Deutschland GmbH Report No. MPPM203-00003-09 Non-GLP/Unpublished	Yes	[redacted]
6.7-06/07/08	Gerharz, T	2014	Determination of the antimicrobial effects of Sporgard WB and Fludioxonil against fungi Internal No. M 2012-32-3, M2011-63 Lanxess Deutschland GmbH Report No. NA Non-GLP/Unpublished	Yes	[redacted]
6.7-06/07/08	Rech M	2013	Method: Determination of the Minimal Inhibitory Concentration (MIC) of test substances against bacteria and fungi Lanxess Deuschland GmbH Report No. M 2 02-00012-12D Non-GLP/Unpublished	Yes	[redacted]
8.1-01	[redacted]	2007	Thiabendazole/azoxystrobin/fludioxonil SC (225.1/225.1/022.7) (A15996A) – Primary skin irritation in rabbits. [redacted] Report No. 21860 GLP/Unpublished	Yes	[redacted]
8.2-01	[redacted]	2007	Thiabendazole/azoxystrobin/fludioxonil SC (225.1/225.1/022.7) (A15996A) – Primary eye irritation in rabbits. [redacted] Report No. 21859 GLP/Unpublished	Yes	[redacted]
8.3-01	[redacted]	2007	Thiabendazole/azoxystrobin/fludioxonil SC (225.1/225.1/022.7) (A15996A) – Dermal sensitisation test – Buehler method. [redacted] Report No. 21861 GLP/Unpublished	Yes	[redacted]
8.5.1-01	[redacted]	2007	Thiabendazole/azoxystrobin/fludioxonil SC (225.1/225.1/022.7) (A15996A) – Acute oral toxicity up-and-down procedure in rats. [redacted] Report No. 21856 GLP/Unpublished	Yes	[redacted]

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8.5.2-01	[redacted]	2007	Thiabendazole/azoxystrobin/fludioxonil SC (225.1/225.1/022.7) (A15996A) – Acute inhalation toxicity in rats [redacted] Report No. 21858 GLP/Unpublished	Yes	[redacted]
8.5.3-01	[redacted]	2007	Thiabendazole/azoxystrobin/fludioxonil SC (225.1/225.1/022.7) (A15996A) – Acute dermal toxicity in rats. [redacted] Report No. 21857 GLP/Unpublished	Yes	[redacted]