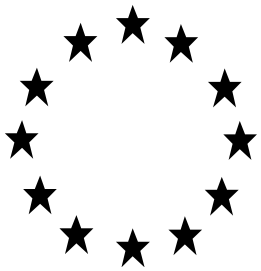
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Dichlofluanid

Product-type 21
(Antifouling Products)

November 2016

UK

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

This assessment report has been established as a result of the evaluation of the active substance dichlofluanid as product-type 21 (antifouling products), carried out in the context of the work programme for the review of existing active substances provided for in Article 89 of Regulation (EU) No 528/2012, with a view to the possible approval of this substance.

Dichlofluanid (CAS no. 1085-98-9) was notified as an existing active substance, by Lanxess Deutschland GmbH, hereafter referred to as the applicant, in product-type 21.

Commission Regulation (EC) No 1062/2014 of 4 August 2014[1] lays down the detailed rules for the evaluation of dossiers and for the decision-making process.

On 30/4/2006, the UK competent authority received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 31/10/2006.

On 22/10/2015 the Rapporteur Member State submitted to the Agency (ECHA) and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report (CAR).

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

1.2. Purpose of the assessment report

The aim of the assessment report is to support the opinion of the Biocidal Products Committee and a decision on the approval of dichlofluanid for product-type 21, and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

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

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.

[1] COMMISSION DELEGATED REGULATION (EU) No 1062/2014 of 4 August 2014 on the work programme for the systematic examination of all existing active substances contained in biocidal products referred to in Regulation (EU) No 528/2012 of the European Parliament and of the Council. OJ L 294, 10.10.2014, p. 1

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

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

The main identification characteristics and the physico-chemical properties of dichlofluanid are given in Appendix I and the 'Confidential Annex' document. The evaluation has established that for the active substance notified by Lanxess Deutschland GmbH none of the manufacturing impurities are considered to be of potential concern.

The methods of analysis for the active substance as manufactured, and for the determination of impurities, have been validated. The methods for analysis in environmental matrices, as appropriate for the areas of use assessed, have been validated and shown to be sufficiently sensitive with respect to the levels of concern.

2.1.2. Intended Uses and Efficacy

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

Dichlofluanid is an active substance proposed for use as an antifoulant in Product Type 21 of the Biocidal Products Regulation.

The active substance has been evaluated for non-professional use only, to be applied by brush or roller to the hulls of pleasure craft.

Dichlofluanid has a broad spectrum of activity which includes algae, diatoms and other fouling organisms.

Anti-fouling products containing dichlofluanid are typically applied at an application rate of 40 – 43 μm dry film thickness.

Regarding mode of action, the biocidal activity of N-haloalkylthio compounds like dichlofluanid is based on the ability of the N-S bond to open and react with nucleophilic entities within the cell such as SH groups of enzymes. Such reactions proceed by way of several steps and lead to disulphides.

Regarding resistance, due to the unspecific mode of action the development of resistance is neither to be expected nor has been ever observed. In addition a literature search regarded to resistance with respect to dichlofluanid and wood preservation was negative. The Fungicide Resistance Action Committee (FRAC) lists recently (2003-06-02) dichlofluanid in group M5 (= multi-site contact activity / sulphamides) together with the comment "generally considered a low risk group with no signs of resistance developing to the majority of fungicides / No cross resistance between the group members".

In addition both the rapid degradation of the active in seawater and freshwater after its release from the paints and the mobility of the treated ship vessels do not provide conditions which would support developing resistances.'

The active substance has been evaluated for non-professional use only, to be applied by brush or roller to the hulls of pleasure craft.

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

2.1.3. Classification and Labelling

The classification and labelling for dichlofluanid according to Regulation (EC) No 1272/2008 (CLP Regulation) is (agreed in RAC opinion on 3 June 2015, however the harmonised classification and labelling in Annex VI of CLP has not been amended yet):

Table 2.1 Current classification of dichlofluanid based on CLP Regulation 1272/2008

Pictogram:	
Signal word:	Warning
Classification:	Acute Tox. 4 Eye Irrit. 2 Skin Sens. 1 Aquatic Acute 1
H-Statements:	H332: Harmful if inhaled H319: Causes serious eye irritation H317: May cause an allergic skin reaction H400: Very toxic to aquatic life
M-Factor (for environmental classification):	Acute M-factor: 10

Based on the available data, the evaluating Competent Authority proposes the following amendment of the existing harmonised classification:

Table 2.2 Proposed classification of dichlofluanid based on CLP Regulation 1272/2008

Pictogram:	
Signal Word:	Warning
Classification:	Acute Tox. 4 Eye Irrit. 2 Skin Sens. 1 Aquatic Acute 1 Aquatic chronic 1
H-Statements:	H332: Harmful if inhaled H319: Causes serious eye irritation H317: May cause an allergic skin reaction H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long-lasting effects
M-Factors (for environmental classification):	M = 10 (acute) M = 10 (chronic)

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

Dichlofluanid is an existing biocide active substance. This PT21 assessment is based primarily on the assessment performed and agreed for dichlofluanid under PT8, updated and revised as necessary.

Dichlofluanid is a white to slightly yellow, crystalline solid with a weak characteristic (musty) odour. The minimum purity of the active substance as manufactured is 960 g/kg dichlofluanid and there are no relevant impurities of toxicological significance.

Dichlofluanid acts as an active and co-active in antifouling paints formulated to protect commercial and pleasure craft and immersed objects/structures against the effects of algae and other organisms like diatoms.

Two representative products have been submitted for evaluation: Alukote A (dichlofluanid only: 4.04% w/w wet paint) and Interspeed Ultra Variant (Copper oxide: 44.27% w/w wet paint and dichlofluanid 2.94% w/w wet paint). Both of these products use dichlofluanid at concentrations typical of products used on pleasure craft and are designed for application by non-professional users. Illustrative risk assessments have been performed for these two products.

The risk characterisation follows the principles described in the *ECHA guidance on the biocidal products regulation, Volume III, Human Health – Part B – risk assessment; Version 1.1* (ECHA, 2015) The risk characterisation for systemic effects is conducted by comparison of the exposure and the toxicity by the Acceptable Exposure Limit (AEL) approach for systemic toxicity. In this approach, the systemic exposure estimates are compared with the determined systemic AEL = N(L)OAEL (mg/kg bw/day)/overall Assessment Factor (AF). Risks are considered acceptable if the Exposure/AEL ratio is < 1 (or <100%). For local effects a risk characterisation has been conducted using a qualitative approach, as described in the ECHA Guidance, Vol III section 4.3.2. (ECHA, 2015).

2.2.1.1. Hazard identification and effects assessment

2.2.1.1.1. *Toxicology hazard summary*

The potential human health effects of dichlofluanid have been well investigated, almost exclusively in experimental animals. The majority of critical studies complied with agreed EU or OECD test protocols applicable at the time of performance and contained documentation of GLP compliance.

Toxicokinetics

The toxicokinetics of dichlofluanid have been well investigated in rats, but not in any other species. Dichlofluanid is rapidly and extensively absorbed (70-90%) from the gastrointestinal tract with the peak plasma concentration occurring from 1.5 to 3.0 hours post-dose. An oral absorption value of 100% has been used in the risk characterisation. As dichlofluanid is almost completely absorbed from the gastrointestinal tract, it is predicted that it will also be well absorbed from the respiratory tract. This prediction is supported by the single inhalation exposure toxicodynamic study in rats, which provides qualitative evidence that dichlofluanid might be systemically available following exposure via this route. An inhalation absorption value of 100% has been used in the risk characterisation of dichlofluanid.

The *in vitro* dermal penetration study on the dichlofluanid representative product,

Interspeed Ultra Variant, suggests 12% of the applied dose was absorbed through the skin (see Document II-B, Section 4.1). Therefore a dermal absorption value of 12% will be used in the risk characterisation for both products in respect of active substance approval. It was agreed at WG III 2016 that at product authorisation, further information on dermal absorption should be provided, taking account of guidance on the dermal absorption of PT21 products, which is being developed.

Orally administered dichlofluanid is rapidly and extensively metabolised, with no parent compound detected systemically. Elimination of radiolabelled dichlofluanid was rapid, with the majority (>90%) of the administered radioactivity cleared via urine during the first 48 hours.

In relation to exposure of the foetus, dichlofluanid metabolites are widely distributed, therefore *in utero* exposure is possible. Exposure of the newborn via the breast milk is considered unlikely, given the rapid and extensive metabolism of dichlofluanid to water-soluble metabolites; it is therefore unlikely to be soluble in the lipid matrix of breast milk.

Acute toxicity, irritancy and sensitisation

Dichlofluanid is of low acute toxicity by the oral and dermal routes of exposure but has moderate acute toxicity by the inhalation route. The data support classification of dichlofluanid for acute toxicity by the inhalation route (Classification, Labelling and Packaging of Substances and Mixtures Regulation 1272/2008 (CLP) - Acute Tox 4; H332).

Dichlofluanid is not classified as a skin irritant, but it does meet the criteria for classification as an eye irritant (CLP – Eye Irrit. 2; H319).

There is evidence that dichlofluanid can cause some respiratory tract irritation; however, the strength of evidence does not meet the EU criteria for classification for this endpoint. Therefore this effect is not considered to be key and is not taken forward to risk characterisation.

Positive findings from guinea pig sensitisation studies demonstrated that dichlofluanid has skin sensitisation potential and meets the EU criteria for classification (CLP – Skin Sens. 1; H317). There is insufficient information to determine whether or not dichlofluanid can cause respiratory sensitisation/occupational asthma, but no such effects have been reported from workers potentially exposed to dichlofluanid.

Acute toxicity studies are available for both non-professional representative products with the exception of an inhalation study for Alukote A. These data, plus the calculation method of the CLP legislation indicate that classification for acute toxicity is not required for either product therefore these endpoints do not need to be considered further at product authorisation. Skin and eye irritation studies are available for each non-professional representative product. These data indicate that Alukote A is a skin and eye irritant and Interspeed Ultra Variant is an eye irritant. Positive results were also observed in a skin sensitisation study on Alukote A, and Interspeed Ultra Variant is also considered to be a skin sensitiser. Local assessments were performed for irritation and sensitisation.

Repeated dose toxicity

The repeat dose toxicity of dichlofluanid via the oral route has been investigated in Rats (120 days to 2 years); dogs (90 days – 2 years) and mice (2 years). A 28 day dermal toxicity study has been performed in rats. There are no studies in experimental animals that address the repeated dose toxicity of dichlofluanid by the inhalation route.

Following repeated oral administration of dichlofluanid, the most prominent finding was fluorosis likely caused by the release of fluoride from the dichlofluanid molecule during its metabolism. This resulted in skeletal osteosclerosis, observed in lifetime dietary studies in both rats and mice. LOAELs of 9.4 and 50.1 mg/kg bw/day for fluorosis were identified in rats and mice respectively. Chronic nephropathy was also observed following repeated oral administration, but in dogs only. The mode of action for the nephropathy is uncertain and possible explanations include direct nephrotoxicity of the active substance or a secondary consequence of elevated systemic fluoride levels. The NOAEL for kidney effects obtained in the 1-year dog study was 2.5 mg/kg bw/day. The same NOAEL was identified for thyroid effects. Hence, any risk from thyroid effects is covered by the risk characterisation for nephrotoxicity.

None of these effects occurred at doses relevant for classification.

Mutagenicity

Although some positive results were seen in *in vitro* assays for gene mutation and chromosome aberrations, dichlofluanid was negative in a range of *in vivo* studies. The weight of evidence from a number of well-conducted *in vitro* and *in vivo* genotoxicity studies indicates that dichlofluanid is not genotoxic *in vivo*.

Carcinogenicity

The carcinogenicity of dichlofluanid was investigated in well performed, 2 year studies in rats and mice. Dichlofluanid induced a slight increase in thyroid tumours in rats at high doses (>300 mg/kg bw/day). Investigative studies indicated that the mode of action was one not considered to be relevant for human health by the EU Specialised Expert (ECB, 1999). No increase in tumour incidence was observed in mice. Overall, dichlofluanid does not show any carcinogenic potential of relevance to human health.

Reproductive toxicity

The potential reproductive toxicity of dichlofluanid was investigated in three, multigeneration, reproductive toxicity studies in rats. Developmental toxicity was investigated in rats and rabbits. Dichlofluanid did not affect mating, fertility. Neither did it cause specific developmental toxicity. A NOAEL of 7-16 mg/kg/day was identified for both parental and offspring toxicity from the 2-generation studies. The rabbit appeared more sensitive than the rat to the effects of dichlofluanid in developmental toxicity studies. A NOAEL of 30 mg/kg/day for maternal/developmental toxicity was identified in the rabbit study.

Endocrine effects

There were no significant effects relevant to humans on endocrine organs and/or reproduction in standard mammalian toxicity studies. Thyroid toxicity, seen at high doses also producing a range of other toxicities, was by a mode of action (thyroid peroxidase inhibition) considered by EU experts (ECB, 1999) to be not relevant for formation of tumours in humans. Instances of testicular degeneration were noted in the 1-year study in beagle dogs, at 37.5 mg/kg/day a dose that produced body weight deficits. In contrast, increased interstitial tissue, but not testicular degeneration was reported at doses of up to 34 mg/kg/day in a longer dog study of two years. No testicular toxicity was observed in repeated dose studies in rats and mice. It was also noted that no effects on fertility were observed in rat multigeneration studies at doses of up to 590-780 mg/kg/day. Adrenal zona fasciculata vacuolation was seen in the 2 year dog study only at a dose level also producing poor condition and body weight deficits. It is therefore concluded that dichlofluanid does not have specific endocrine-disrupting properties relevant to a human health risk

assessment. In addition, the available toxicity data do not support classification of dichlofluanid in category 2 for reproductive toxicity and category 2 for carcinogenicity (CLP). Therefore, the interim criteria for endocrine disruptors are not met.

2.2.1.1.2. *Critical endpoints and AEL derivation*

The relevant information for the risk characterisation for exposure to dichlofluanid comes largely from oral studies. No data are available to assess systemic toxicity via the inhalation route and, in the only dermal study that is available (28-day study in rats), there were no signs of systemic toxicity at the highest dose tested (1000 mg/kg/day). Toxicokinetic studies indicate that there does not appear to be significant first-pass metabolism, so following absorption, similar toxicokinetic and toxicodynamic profiles of dichlofluanid would be expected after oral, dermal and inhalation exposures. Overall, use of oral studies for the derivation of systemic AELs for dichlofluanid is considered appropriate for inhalation and dermal exposure.

Acute AEL

An acute AEL (i.e. estimated human exposure ≤ 24 h) was not identified in the risk characterisation of dichlofluanid under PT8 as a different approach to risk characterisation was taken at that time. Taking into account all of the available data, and the absence of any appropriate single dose studies, the UK CA considers the NOAEL of 30 mg/kg/day for maternal/developmental toxicity identified in the rabbit developmental study to be the most appropriate starting point for the derivation of an acute AEL.

There is no information available to identify the relative sensitivities of rabbits and humans in relation to the toxicity of dichlofluanid. Similarly, there are no data to reliably inform on the potential for inter-individual variability in susceptibility to the effects of dichlofluanid. Therefore, standard assessment factors (AF) to account for potential inter-species (AF = 10) and intra-species (AF = 10) variability need to be included in the risk characterisation.

AEL $_{Acute}$ = 0.3 mg/kg bw/day (30 mg/kg bw/day/overall AF of 100)

Medium term and Long term AEL

In the risk characterisation of dichlofluanid under PT8, two critical effects, skeletal osteosclerosis (fluorosis) and chronic nephropathy, observed in rats and dogs respectively were assessed against each long term exposure scenario. These effects are also considered relevant to the risk characterisation of dichlofluanid under PT21 for both medium term and long term exposure scenarios.

Fluorosis

The toxicokinetic studies show that fluoride is released from the parent molecule. The bones and teeth will take up any bioavailable fluoride, if the body burden is sufficiently high and exposure is sufficiently prolonged. If the degree of such uptake is excessive, it can lead to skeletal osteosclerosis. This explains the mechanism behind the observed skeletal osteosclerosis seen in rodents. It is possible that the kidney toxicity seen in dogs is also a consequence of the excess fluoride, especially as fluoride is excreted via the kidneys. However, there is no direct information to confirm this possibility. Given this uncertainty, the kidney changes should be considered as a separate effect.

In the lifetime oral study in rats, skeletal osteosclerosis was observed at all doses; therefore it was not possible to identify a NOAEL for this effect. A LOAEL of 9.4-13.5 mg/kg/day was established, which was the lowest dose used. However, the fact that a NOAEL was not established is not critical as there are extensive data on the systemic effects of fluoride on humans.

In humans, prolonged environmental exposure to high levels of fluoride causes adverse dental changes as well as skeletal changes. There are human data which indicate that intakes above 0.05 mg fluoride/kg/day will cause moderate dental fluorosis (COT, 2003); and human population studies which indicate that skeletal fluorosis occurs following prolonged environmental exposure, at intakes of around 0.1-0.23 mg fluoride/kg/day (IPCS, 2002). Therefore, elevated fluoride levels are of concern for human health. The EFSA NDA Panel proposed a tolerable upper level for fluoride intake at 0.12 mg/kg bw/day (EFSA, 2005).

Taking into account the human data, a NOAEL of 0.05 mg fluoride/kg/day is identified for fluorosis. In the UK, the Total Dietary Survey found the average adult dietary intake to be around 0.02 mg fluoride/kg/day (COT, 2003). Therefore, the NOAEL for fluorosis should be adjusted to 0.03 mg fluoride/kg/day to take account of background levels of dietary intake. The adjusted NOAEL of 0.03 mg fluoride/kg/day is equivalent to 0.53 mg dichlofluanid/ kg/day (assuming dichlofluanid contains 5.7% by weight of fluoride and 100% fluoride is released from dichlofluanid during metabolism – dichlofluanid has a molecular wt of 333 and contains one fluorine atom).

As this NOAEL is based on human population-based studies there is no need for an assessment factor to account for interspecies variability. Also, intraspecies variability is already accommodated within such data.

Overall, a medium term and a long term AEL for dichlofluanid of 0.53 mg/kg/ bw/day can be derived from the data on fluorosis.

Nephrotoxicity

Nephrotoxicity has been observed in studies in dogs. The mode of action for the nephropathy is uncertain and possible explanations include direct nephrotoxicity of the active substance or a secondary consequence of elevated systemic fluoride levels. In either case, dichlofluanid-mediated nephrotoxicity in dogs is potentially relevant for human health. In the 1-year oral study in dogs, a NOAEL of 2.5 mg/kg/day was identified for minimal to moderate chronic nephropathy.

There is no information available to identify the relative sensitivities of dogs and humans in relation to the toxicity of dichlofluanid. Similarly, there are no data to reliably inform on the potential for inter-individual variability in susceptibility to this effect. Therefore, standard assessment factors (AF) to account for potential inter-species (AF = 10) and intra-species (AF = 10) variability need to be included in the risk characterisation.

Overall, a medium term/long term AEL of 0.025 mg/kg/bw/day can be derived from the data on nephrotoxicity.

The AEL derived from the data on nephrotoxicity clearly produces the more conservative AEL than that for fluorosis therefore the medium term and long term AEL is 0.025 mg/kg bw/day.

AEL $_{\text{Medium term}}$ = 0.025 mg/kg bw/day (2.5 mg/kg bw/day/overall AF of 100)

AEL $_{\text{Long term}}$ = 0.025 mg/kg bw/day (2.5 mg/kg bw/day/overall AF of 100)

Dietary risk assessment – ADI and ARfD

There is the potential for residues of dichlofluanid used as antifoulant to occur in food and feed of marine origin. Therefore, an ADI and ARfD have been derived. Dichlofluanid does not have an ADI or ARfD from EFSA. The JMPR derived an ADI of 0- 0.3 mg/kg bw based on a NOAEL of 25 mg/kg bw/day in the 1 year dog study. As the conclusion on the 1 year dog study in the PT8 CAR was that the NOAEL is 2.5 mg/kg bw/day the UK CA proposes to derive an ADI using the same basis as the long-term AEL. For the ARfD the approach used for the acute AEL is proposed.

ADI = 0.025 mg/kg bw (2.5 mg/kg bw/day; AF of 100)

ARfD = 0.3 mg/kg bw (30 mg/kg bw/day; AF of 100)

At product authorisation, a more refined risk assessment might be required. Also, if necessary, the establishment of maximum residue levels (MRLs) should be considered.

Local effects

Dichlofluanid is classified for eye irritation and skin sensitisation (H319, H317). 'Alukote A' is classified for skin and eye irritation and skin sensitisation (H315, H319, H317). 'Interspeed Ultra Variant' is classified for eye irritation (H319). A qualitative risk characterisation will therefore be performed based on Section 4.3.2 of the ECHA guidance (ECHA, 2015).

2.2.1.2. Exposure assessment

Two products have been submitted for evaluation: 'Alukote A' (dichlofluanid only: 4.04% w/w wet paint) and 'Interspeed Ultra Variant' (Copper oxide: 44.27% w/w wet paint and dichlofluanid 2.94% w/w wet paint). 'Alukote A' and 'Interspeed Ultra Variant' are Controlled Depletion Polymer (CDP) type antifouling paints designed for use on pleasure craft in fully saline and estuarine waters. Both of these are designed for application by non-professionals using brush and roller techniques.

Exposures were estimated using a tiered approach as described in the TNsG on Human Exposure to Biocidal Products (2002).

The main paths of human exposure to dichlofluanid resulting from the use of the products 'Alukote A' and 'Interspeed Ultra Variant' are given in the table below:

Summary table: relevant paths of human exposure					
Exposure path	**Primary (direct) exposure**		**Secondary (indirect) exposure**		
	Professional use*	**Non-professional use**	**Professional use***	**General[a] public**	**Via food**
Inhalation	n/a	Yes	n/a	No	No
Dermal	n/a	Yes	n/a	Yes	No
Oral	n/a	No	n/a	Yes	Yes
[a] Includes people other than those applying the product. *Professional use of the products has not been requested.					

Primary and secondary exposure scenarios pertaining to the proposed use of the products 'Alukote A' and 'Interspeed Ultra Variant' are detailed below:

List of exposure scenarios			
Scenario number	**Scenario**	**Primary or secondary exposure Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
1.	Brush and roller application of the product	Primary exposure - an adult applies the product to the surface of the vessel using a brush and/or roller.	Non-professional
2.	Washing out contaminated brushes	Primary exposure - an adult cleans out a brush contaminated with the product using an appropriate solvent.	Non-professional
3.	Paint removal using high pressure water washing and/or abrasion techniques.	Primary exposure - an adult removes the dried paint from the surface of the vessel using high pressure water washing and/or abrasion equipment.	Non-professional
4.	Laundering work clothing	Secondary exposure – an adult launders contaminated (from non-professional application of the product) clothing at home.	Bystanders (general public)
5.	Contact with treated boat surface	Secondary exposure – a young child (toddler) touches a boat surface coated in the product….	Bystanders (general public)
6.	Exposure via the environment	Secondary exposure - an individual may consume fish contaminated with dichlofluanid	General Public

2.2.1.2.1. *Primary exposure*

Professional users

Not applicable. The only uses requested are non-professional uses.

Non-Professional users

Scenarios for primary exposure were application by brush and roller, cleaning of contaminated brushes and paint removal with high pressure washing and abrasion. Full details of the scenarios, tiers and assumptions made can be found in Document IIB Section 3.2.3. The estimated exposures at relevant tiers are given in Tables 2.3 to 2.8. Uses are considered to be one or two days per year and considered to be acute.

'Alukote A' (4.04% dichlofluanid)

Table 2.3 Primary exposure to dichlofluanid to a non-professional user during the brush and roller application of the product 'Alukote A' (4.04% w/w dichlofluanid)

Tier	PPE	Inhalation uptake (mg a.s./kg bw/day	Dermal uptake (mg a.s./kg bw/day	Oral uptake (mg a.s./kg bw/day	Total systemic dose (mg a.s / kg bw/day)
1	None.	0.000095	1.1704	n.a.	1.1705
2	None.	0.000063	0.7802	n.a.	0.7803
3	Protective gloves only.	0.000063	0.3578	n.a.	0.3578
4	Protective gloves, 'normal' long sleeved shirt, trousers and shoes.	0.000063	0.2461	n.a.	0.2462

'Interspeed Ultra Variant' (2.94% w/w dichlofluanid)

Table 2.4 Primary exposure to dichlofluanid a non-professional user during the brush and roller application of the product 'Interspeed Ultra Variant' (2.94% w/w dichlofluanid)

Tier	PPE	Inhalation uptake (mg a.s./kg bw/day	Dermal uptake (mg a.s./kg bw/day	Oral uptake (mg a.s./kg bw/day	Total systemic dose (mg a.s / kg bw/day)
1	None.	0.000068	0.8517	n.a.	0.8518
2	None.	0.000047	0.5678	n.a.	0.5679
3	Protective gloves only.	0.000047	0.2604	n.a.	0.2604
4	Protective gloves, 'normal' long sleeved shirt, trousers and shoes.	0.000047	0.1791	n.a.	0.1792

Table 2.5 Primary exposure to dichlofluanid for a non-professional user washing brushes used to apply 'Alukote A' (4.04% w/w dichlofluanid)

Tier	PPE	Dermal uptake after 1st wash (mg a.s./person)	Dermal uptake after 2nd wash (mg a.s. /person)	Dermal uptake after 3rd wash (mg a.s. /person)	Total systemic dose (mg a.s. /kg bw/event)
1	None	0.8399	0.0420	0.0021	0.0147
2	Gloves only	0.0840	0.0042	0.0002	0.0015

Table 2.6 Primary exposure to dichlofluanid for a non-professional user washing brushes used to apply 'Interspeed Ultra Variant' (2.94% w/w dichlofluanid)

Tier	PPE	Dermal uptake after 1st wash (mg a.s./person)	Dermal uptake after 2nd wash (mg a.s. /person)	Dermal uptake after 3rd wash (mg a.s. /person)	Total systemic dose (mg a.s. /kg bw/event)
1	None	0.7131	0.0357	0.0018	0.0125
2	Gloves only	0.0713	0.0036	0.0002	0.0013

Table 2.7 Primary exposure to dichlofluanid to a non-professional removing the dried product 'Alukote A' by high-pressure water washing or abrasion (rubbing with a wire brush)

Tier	PPE	RPE	Duration (mins)	Exposure to dichlofluanid (total systemic dose in mg a.s./kg bw/day)
1	None – no gloves or clothing	None	135	0.1846
2	None – no gloves or clothing	None	90	0.1230
3	Protective gloves	None	90	0.0564
4	Protective gloves with 'normal' long sleeved clothing, trousers and shoes (default 50 % penetration)	None	90	0.0388
Note: this model overestimates exposure for non-professionals removing antifouling paint by high-pressure water washing or abrasion (rubbing with a wire brush).				

Table 2.8 Primary exposure to dichlofluanid to a non-professional removing the dried product 'Interspeed Ultra Variant' by high-pressure water washing or abrasion (rubbing with a wire brush)

Tier	PPE	RPE	Duration (mins)	Exposure to dichlofluanid (total systemic dose in mg a.s. /kg bw/day)
1	None – no gloves or clothing	None	135	0.1130
2	None – no gloves or clothing	None	90	0.0753
3	Protective gloves	None	90	0.0345
4	Protective gloves with 'normal'	None	90	0.0238

	long sleeved clothing, trousers and shoes (default 50 % penetration)			
Note: this model overestimates exposure for non-professionals removing antifouling paint by high-pressure water washing or abrasion (rubbing with a wire brush).				

2.2.1.2.2. *Secondary exposure*

Secondary exposure scenarios have been evaluated for the following activities:

- Laundering work clothing – dermal contact
- Young child (toddler) touching the treated boat and contacts wet paint – dermal and hand to mouth.
- Young child (toddler) touching the treated boat and contacts dry paint– dermal and hand to mouth
- Consumption of fish.

Full details of the exposure modelling for the scenarios are presented in Section 3.2.5 of Volume IIB. Because of the limited use of antifouling paints by non-professional users (1 day, once or twice per year) the exposures are considered to be acute in nature. The fish consumption values are based on the worst case PEC in Swiss marina fish. Results of the exposure predictions are presented in Tables 2.9 to 2.15.

Table 2.9 Total systemic exposure to dichlofluanid for an individual washing work clothing contaminated with the product 'Alukote A'

Tier	Individual Exposed	Dermal uptake (mg a.s./kg bw/day)	Total systemic exposure (mg a.s. /kg bw/day)
1	Adult	0.0255	0.0255
2	Adult	0.0170	0.0170

Table 2.10 Total systemic exposure to dichlofluanid for an individual washing work clothing contaminated with the product 'Interspeed Ultra Variant'

Tier	Individual Exposed	Dermal uptake (mg a.s./kg bw/day)	Total systemic exposure (mg a.s. /kg bw/day)
1	Adult	0.0186	0.0186
2	Adult	0.0124	0.0124

Table 2.11 Total systemic exposure to dichlofluanid for a child touching a treated boat surface and contacting wet 'Alukote A' paint

Tier	Individual Exposed	Dermal uptake (mg a.s./kg bw/day)	Oral uptake (mg a.s./kg bw/day)	Total systemic exposure (mg a.s. /kg bw/day)
1	Child	0.7741	0.6451	1.4192

Table 2.12 Total systemic exposure to dichlofluanid for a child touching a treated boat surface and contacting wet 'Interspeed Ultra Variant' paint

Tier	Individual Exposed	Dermal uptake (mg a.s./kg bw/day)	Oral uptake (mg a.s./kg bw/day)	Total systemic exposure (mg a.s. /kg bw/day)
1	Child	0.6640	0.5530	1.217

Table 2.13 Total systemic exposure to dichlofluanid for a child touching a treated boat surface and contacting dried 'Alukote A' paint

Tier	Individual Exposed	Dermal uptake (mg a.s./kg bw/day)	Oral uptake (mg a.s./kg bw/day)	Total systemic exposure (mg a.s. /kg bw/day)
1	Child	0.0293	0.1219	0.1511

Table 2.14 Total systemic exposure to dichlofluanid for a child touching a treated boat surface and contacting dried 'Interspeed Ultra Variant' paint

Tier	Individual Exposed	Dermal uptake (mg a.s./kg bw/day)	Oral uptake (mg a.s./kg bw/day)	Total systemic exposure (mg a.s. /kg bw/day)
1	Child	0.0210	0.0873	0.1083

Table 2.15 Quantity of fish that an individual would need to consume to equal the ADI for dichlofluanid

Individual	**Infant**	**Toddler**	**Child**	**Adult**
ADI (mg/kg bw/day)	0.025	0.025	0.025	0.025
Body weight (kg)	8	10	23.9	60
PEC (mg/kg wet fish)	1.22×10^{-2}	1.22×10^{-2}	1.22×10^{-2}	1.22×10^{-2}
Weight of wet fish to be consumed <u>in a day</u> (kg) to equal the ADI	**16**	**21**	**49**	**123**

2.2.1.2.3. *Combined exposure*

The UK CA considers it possible that the following activities might be performed by the same person on the same day:

- Application of new paint (brush / roller)
- Washing of brushes

Dietary exposures are discounted as they will be trivial.

The predicted combined exposures from these activities are presented in Table 2.16 and 2.17 below, for 'Alukote A' and 'Interspeed Ultra Variant' respectively.

Table 2.16 Combined exposures pertaining to the product 'Alukote A'

Scenario	Tier	PPE/Clothing	Total Systemic Exposure (mg a.s./kg bw)
			Adult
Total systemic exposure during application (brush and roller) of the product to the hull of a pleasure craft	4	Gloves with normal clothing	0.2462
Total systemic exposure during the cleaning of a contaminated brush	1	None	0.0147
Total systemic exposure			0.2609
Combined total exposure as % acute AEL of 0.3 mg/kg bw			**87%**

Table 2.17 Combined exposures pertaining to the product 'Interspeed Ultra Variant'

Scenario	Tier	PPE/Clothing	Total Systemic Exposure (mg a.s./kg bw)
			Adult
Total systemic exposure during application (brush and roller) of the product to the hull of a pleasure craft	4	Gloves with normal clothing	0.1792
Total systemic exposure during the cleaning of a contaminated brush	1	None	0.0125
Total systemic exposure			0.1917
Combined total exposure as % acute AEL of 0.3 mg/kg bw			**64%**

2.2.1.3. Risk characterisation

2.2.1.3.1. *Primary exposure*

Systemic effects

Non-professional users of the products 'Alukote A' and 'Interspeed Ultra Variant' are expected to apply the products for a period of 90 minutes on one, or possibly two days of the year. Given this exposure scenario it is considered that the most relevant reference dose for all exposure scenarios is the acute AEL of 0.3 mg/kg bw/day. A dermal absorption value of 12% is used for all scenarios.

Primary total systemic exposure to dichlofluanid (in different scenarios), resulting from the use of the non-professional products, 'Alukote A' and 'Interspeed Ultra Variant', has been compared with the short-term AEL value of 0.3 mg/kg bw/d. Tables 2.18 & 2.19 below, summarise these comparisons for the different scenarios.

Table 2.18 Exposure and risk characterisation for the use of 'Alukote A' (4.04% w/w dichlofluanid)

Scenario	Tier	Total systemic exposure (mg/kg bw/d)	Relevant AEL for general public (mg/kg bw/d)	Exposure /AEL (%)	Acceptable risk?
Brush and roller application	Tier 1	1.1705	0.3	390	No
	Tier 2	0.7803	0.3	260	No
	Tier 3	0.6687	0.3	223	No
	Tier 4	0.2462	0.3	82	**Yes**
Cleaning paint brushes	Tier 1	0.0147	0.3	5	**Yes**
	Tier 2	0.0015	0.3	<1	**Yes**
Paint removal (high pressure washing or abrasion)	Tier 1	0.0738	0.3	25	**Yes**
	Tier 2	0.0492	0.3	16	**Yes**
	Tier3	0.0422	0.3	14	**Yes**
	Tier 4	0.0156	0.3	**5**	**Yes**

Table 2.19 Exposure and risk characterisation for the use of 'Interspeed Ultra Variant' (2.94% w/w dichlofluanid)

Scenario	Tier	Total systemic exposure (mg/kg bw/d)	Relevant AEL for general public (mg/kg bw/d)	Exposure /AEL (%)	Acceptable risk?
Brush and roller application	Tier 1	0.8518	0.3	284	No
	Tier 2	0.5679	0.3	189	No
	Tier 3	0.4866	0.3	162	No
	Tier 4	0.1792	0.3	60	**Yes**
Cleaning paint brushes	Tier 1	0.0125	0.3	4	**Yes**
	Tier 2	0.0013	0.3	<1	**Yes**
Paint removal (high pressure washing or abrasion)	Tier 1	0.0452	0.3	15	**Yes**
	Tier 2	0.0301	0.3	10	**Yes**
	Tier3	0.0258	0.3	9	**Yes**
	Tier 4	0.0095	0.3	**3**	**Yes**

As shown in Table 2.18 above, the predicted exposure to 'Alukote A' during application is below the AEL for Tier 4. This is based on a 90 minute exposure, protection from normal clothing and the use of gloves. Predicted exposures for brush washing and paint removal are below the AEL at Tier 1 (no protection from clothing). The risks associated with systemic exposures arising from the application of 'Alukote A' by non-professionals are considered to be acceptable.

As shown in Table 2.19 above, the predicted exposure to 'Interspeed Ultra Variant' during application is below the AEL for Tier 4. This is based on a 90 minute exposure, protection from normal clothing and the use of gloves. Predicted exposures for brush washing and paint removal are below the AEL at Tier 1 (no protection from clothing). The risks associated with systemic exposures arising from the application of 'Interspeed Ultra Variant' by non-professionals are considered to be acceptable.

Local effects

1) Alukote A' is classified for skin and eye irritation (both Cat 2) and skin sensitisation (Cat 1B).

Eyes

The results for eye irritation are difficult to interpret due to the non-standard, low volume study protocol used, in which mild effects were seen. The skin irritation results were marked and had not reversed 14 days after exposure, indicating a potential for severe eye irritation or damage. 'Alukote A' is viscous and the UK CA considers it unlikely that significant contamination of the eye would occur. However, the uncertainties about the outcome of any eye contamination during application require mitigation. In the opinion of the UK CA this can be provided by including label phrases advising the use of **eye protection** (P280) and advice to avoid eye exposure (P262) and to rinse eyes in the event of contamination (P305+ 351+338) .

Skin

The skin irritation results with 'Alukote A' were marked and had not reversed 14 days after exposure (Section 4.3.1.1 of Document IIB). The exposures were for 4 hours under semi-occlusive conditions, which are much more severe than the predicted use of 'Alukote A' (90 minutes, mainly unoccluded exposure). Skin sensitisation is also a significant risk as approximately 50% of guinea pigs responded to a 1% solution of 'Alukote A' in a maximisation test. 'Alukote A' is viscous and the UK CA considers it unlikely that significant contamination of the skin would occur. However some skin contamination from splashes and droplets is plausible. The UK CA considers that the risks to can be adequately mitigated by the use of **gloves** (P280) and advice to avoid skin exposure (P262) and to wash contaminated skin (302+352).

Respiratory tract

There are no data on the potential of 'Alukote A' to produce respiratory irritation or sensitisation. Given the findings for skin irritation and skin sensitisation, respiratory irritation and sensitisation cannot be discounted. The physical properties of the product (viscous paint) and method of application (brush or roller) should mean that there will be few if any inhalable particles and therefore the risks for local effect on the respiratory tract are considered to be acceptable.

Conclusion for 'Alukote A'

The risks of local effects to eyes, skin and respiratory tract, from the brush and roller

application of 'Alukote A', are considered acceptable with the inclusion of the following phrases on the label:

Do not get in eyes or on skin (P262)
Wear gloves and eye protection when applying (P280)
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses if present and easy to do – continue rinsing (P305+ 351+338)
IF ON SKIN: Wash with soap and water. (P302+352)

2) 'Interspeed Ultra Variant' is classified as irritating to eyes (Cat 2) and skin sensitisation (Cat 1B).

Eyes

The results for the eye irritation showed that 'Interspeed Ultra Variant' was a moderate eye irritant with some persistence as the exposed eyes took 8 days to fully recover. 'Interspeed Ultra Variant' is viscous and the UK CA considers it unlikely that significant contamination of the eye would occur. Should it occur, the effects although initially marked in terms of conjunctival redness are expected to be fully reversible. In the opinion of the UK CA the risks to eyes are acceptable without the use of eye protection. Label phrases giving advice to avoid exposure of the eye (P262) and to rinse contaminated eyes (P305+ 351+338) are considered appropriate.

Skin

'Interspeed Ultra Variant' is classified for skin sensitisation. The results underlying this conclusion were seen with challenge exposure to undiluted material for 24 or 48 hours under an occlusive dressing but not to challenge with a 50% solution for the same duration. In addition, scabbing was reported in the skin sensitisation study in approximately half the guinea pigs exposed to undiluted product for 24 or 48 hours under an occlusive dressing. The relevance of these findings to human exposures from the application of 'Interspeed Ultra Variant' by brush or roller is unclear given the extreme exposure conditions used. Overall, the UK CA considers that the risks are low and should be acceptable if normal hygienic practices are observed. However, given the sensitisation classification it is the UK CA considers that the risks to can be adequately mitigated by the use of **gloves** (P280) and advice to avoid skin exposure (P262) and to wash contaminated skin (302+352).

Respiratory tract

There are no data on the potential of 'Interspeed Ultra Variant' to produce respiratory irritation or sensitisation. Given the findings for skin irritation and skin sensitisation, respiratory irritation and sensitisation cannot be discounted but is unlikely to be severe. The physical properties of the product (viscous paint) and method of application (brush or roller) should mean that there will be few if any inhalable particles and therefore the risks for local effect on the respiratory tract are considered to be acceptable.

Conclusion for 'Interspeed Ultra Variant'

The risks of local effects to eyes, skin and respiratory tract, from the brush and roller application of 'Interspeed Ultra Variant', are considered acceptable with the inclusion of the following phrases on the label:

Do not get in eyes or on skin (P262)
Wear gloves when applying (P280)
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses if present and easy to do – continue rinsing (P305+ 351+338)
IF ON SKIN: Wash with soap and water. (P302+352)

2.2.1.3.2. *Secondary exposure*

Systemic effects

Secondary total systemic exposure to dichlofluanid (in different scenarios) of members of the public (resulting from the use of the non-professional products, 'Alukote A' and 'Interspeed Ultra Variant') has been compared with the short-term AEL value of 0.3 mg/kg bw/d. Tables 2.20 & 2.21 below, summarise these comparisons for the different scenarios.

Table 2.20 Risks from secondary systemic exposure to dichlofluanid resulting from the use of the non-professional product 'Alukote A'

Scenario	Tier	Total systemic exposure (mg/kg bw/d)	Short-term AEL (mg/kg bw/d)	Exposure/AEL %	Acceptable risk?
Adult laundering contaminated work clothes	1	0.0255	0.3	9	**Yes**
	2	0.0170	0.3	6	**Yes**
Young child touching <u>wet</u> paint from a boat surface	1	1.4192	0.3	473	No
Young child touching <u>dry</u> paint from a boat surface	1	0.1340	0.3	45	**Yes**

Table 2.21 Risks from secondary systemic exposure to dichlofluanid resulting from the use of the non-professional product 'Interspeed Ultra Variant'

Scenario	Tier	Total systemic exposure (mg/kg bw/d)	Short-term AEL (mg/kg bw/d)	Exposure/AEL %	Acceptable risk?
Adult laundering contaminated work clothes	1	0.0186	0.3	6	**Yes**
	2	0.0124	0.3	4	**Yes**
Young child touching <u>wet</u> paint from a boat surface	1	1.217	0.3	406	No
Young child touching <u>dry</u> paint from a	1	0.0961	0.3	32	**Yes**

boat surface	

For both 'Alukote A' and 'Interspeed Ultra Variant' laundering exposures are below the acute AEL at Tier 1. Young child exposures following contact with dried paint are below the acute AEL at Tier 1.

Young child exposures following contact with wet paint are above the acute AEL at Tier 1. No further refinements are available for the exposure modelling. The UK CA considers that the risks could be mitigated adequately by the use of a warning phrase on the product label:

'KEEP UNPROTECTED PERSONS AND ANIMALS AWAY UNTIL TREATED SURFACES ARE DRY'

Systemic effects from exposure due to the consumption of food are unlikely. Predicted exposures from marine fish are very low, with the ADI not being exceeded even by the consumption of 1 kg fish per kg bw/day. The risks from oral exposures are considered acceptable.

Local Effects

Dichlofluanid is classified for skin sensitisation. 'Alukote A' is classified for skin and eye irritation and skin sensitisation. 'Interspeed Ultra Variant' is classified as irritating to eyes and skin sensitisation. Risks for these local effects from secondary exposure for an adult washing clothes contaminated with either or both products are considered to be acceptable as exposures are likely to be almost negligible and to dried material. Risks of local skin effects, particularly skin sensitisation for a child touching a boat surface treated with 'Alukote A' when the paint is still wet are considered moderate, for 'Interspeed Ultra Variant' these risks are considered low due to skin reactions in the sensitisation test being seen only at concentrations above 50%. However, as for the systemic risks, it is considered that such skin sensitisation risks could be mitigated by an additional warning on the product label:

'KEEP UNPROTECTED PERSONS AND ANIMALS AWAY UNTIL TREATED SURFACES ARE DRY'.

2.2.1.3.3. *Combined exposure*

Tables 2.16 & 2.17 above demonstrate that combined systemic exposures to dichlofluanid arising from 'Alukote A' and 'Interspeed Ultra Variant' are below the acute AEL if gloves and normal clothing are worn during the brush / roller application of new material. These are considered to be reasonable expectations for the activities involved.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Fate in the aquatic compartment (including sediment)

Dichlofluanid hydrolyses rapidly in freshwater and seawater to form N,N-dimethyl-N'-phenylsulfamide (DMSA). It is not considered susceptible to photodegradation but is classed as inherently biodegradable. Dichlofluanid degraded rapidly in natural waters, the DT_{50} was 0.09 days in freshwater (20.5ºC) and 0.05 days in seawater (20ºC). These values were used for modelling purposes as degradation was rapid in the water / sediment studies and it was not possible to calculate DT_{50} values. No dichlofluanid was seen in the sediment therefore, in line with the PT21 guidance, a simple conservative DT_{50} value of 1000 days was used for degradation in the sediment. DMSA was the major degradation product, reaching a maximum of 98.3% AR at day 14. The water phase geomean DT_{50} value of 189.0 days was used for modelling, and again 1000 days for the sediment phase. Although it was

not reported in the water / sediment study for dichlofluanid because the position of the radiolabel precluded its analysis, N,N-dimethylsulfamide (N,N-DMS) was assumed to be formed in a similar way to that seen in the equivalent water / sediment study for the closely related tolylfluanid. In that study N,N-DMS reached a maximum of 78.2% AR and had a DT_{50} > 1000 days in the whole system, water, and sediment phases. For modelling, 1000 days was assigned as the DT_{50} value in both water and sediment. All DT_{50} values were adjusted to the appropriate temperature of the model scenario using Q_{10} = 2.2. Both DMSA and N,N-DMS are hydrolytically stable and DMSA is not readily biodegradable.

Fate in air

Dichlofluanid has a vapour pressure of 2.15 x 10^{-5} Pa and half life in air of about 12.5 hours. These properties and the intended use pattern suggest that exposure of the air compartment is unlikely. DMSA and N,N-DMS also have low vapour pressures and therefore are not expected to partition to the atmosphere to any great extent.

Fate in the terrestrial compartment

In the aerobic soil study, dichlofluanid had a DT_{50} < 1 day and the main metabolite was DMSA. The DT_{50} value for DMSA in soil was estimated at 40 days during the PT8 evaluation of dichlofluanid. Again N,N-DMS formation could not be followed in the aerobic degradation study for dichlofluanid but in an equivalent study for tolylfluanid the maximum percentage soil formation was 23.1% (no DT_{50} determined). The K_{oc} values determined from the adsorption / desorption screening test were 1344 for dichlofluanid and 53 for DMSA. No adsorption of N,N-DMS was seen in any of five different soils tested.

2.2.2.2. Effects assessment

Most of the ecotoxicology assessment has been taken from the dichlofluanid PT 8 CAR, which has already been fully peer reviewed (inc. at TMI06). Key ecotoxicological effects endpoints (inc. PNECs) have previously been accepted for Annex I inclusion of dichlofluanid under the PT 8 assessment. Apart from some minor clarifications, the only changes have been to add effects data recently provided on the metabolite N-N-DMS; some data on marine organisms which may be of relevance to this PT21 assessment and derivation of freshwater and saltwater/marine PNECs.

Aquatic

Dichlofluanid has a high acute toxicity rainbow trout (*Oncorhynchus mykiss*, formerly *Salmo gairdneri*) with an LC_{50} of 0.010 mg a.s./l and a NOEC of < 0.0026 mg a.s./l (LOD) under flow-through conditions (96 h). An additional and reliable acute study on the marine sheepshead minnow (*Cyprinodon variegatus*) has been provided, which gave an LC_{50} (96 h) of 10.54 µg a.s./l. The LC_{50} (96 h) of rainbow trout (*Oncorhynchus mykiss*) exposed to the metabolite N,N-DMS was > 100 mg/l. No acute fish data are available on the main DMSA metabolite.

In acute toxicity studies on *Daphnia magna* with dichlofluanid, the EC_{50} (48 hours) was determined to be 0.42 mg a.s./l. The EC_{50} (48 hours, static) of the main metabolite DMSA was determined to be > 95.6 mg/l. The toxicity of N,N-DMS is low with a 48-hour EC_{50} of > 100 mg/l.

In a test on dichlofluanid performed with the green alga *Scenedesmus subspicatus*, an E_rC_{50} (72 h) of 15 mg a.s./l was obtained for growth rate. The NOEC for growth rate was

determined to be 1.0 mg a.s./l. As these endpoints were reported based on nominal concentrations, a study with the marine diatom *Skeletonema costatum* was also considered for the PNEC derivation of dichlofluanid as its endpoints are related to initial measured concentrations. The study reported a NOEC of 0.64 µg a.s./l based on mean measured concentration. For DMSA, the E_rC_{50} was > 97.7 mg/l and there were no effects at this concentration. N,N-DMS is also of low toxicity to algae indicated by an E_rC_{50} of > 100 mg/l.

Acute toxicity to aquatic micro-organisms was low for both dichlofluanid and DMSA. The calculated EC_{50} values were 9.43 mg a.s./l and 1140 mg/l, respectively. It is noted that the water solubility of dichlofluanid is only 1.3 mg/l.

Longer term studies with fish have also been performed. A prolonged toxicity test with rainbow trout (*O. mykiss*) gave a NOEC after 21 days exposure of 0.00455 mg a.s./l. An early life stage study with the fathead minnow (*Pimephales promelas*) exposed to dichlofluanid resulted in a NOEC of 0.00407 mg a.s./l. For DMSA, the NOEC from a prolonged 21-day toxicity test on rainbow trout was determined to be 10.0 mg/l. No dose-response relationship was observed. In a 28-day juvenile growth test on rainbow trout with N,N-DMS, there were no adverse effects and no metabolite-related mortality observed in any treatment level. The NOEC was therefore 100 mg/l, the highest concentration tested.

A 21-day chronic toxicity study on *Daphnia magna* exposed to dichlofluanid gave a NOEC of 0.00265 mg a.s./l. An additional prolonged acute study on dichlofluanid has been provided using the marine sediment-dwelling amphipod *Corophium volutator*, this gave a NOEC of 0.386 mg a.s./l based on initial measured concentrations in the water phase but is not considered reliable for use in regulatory risk assessment given uncertainty regarding exposure of test organisms over the study duration. For DMSA, a chronic spiked-water study on aquatic invertebrates was performed with sediment dwelling larvae of the midge *Chironomus riparius*. A NOEC was not derived but the lowest EC_{05} was reported to be 7.4 mg/l (in the water phase) for the endpoint 'development rate in males'. In a 21-day *Daphnia* reproduction study with N,N-DMS, a NOEC of 100 mg/l was observed (the highest concentration tested).

Atmosphere

No ecotoxicological data submitted - and not a standard requirement for PT21 assessment.

Terrestrial

Studies on terrestrial plants and earthworms exposed to dichlofluanid have been performed. The EC_{50} for plants exposed to dichlofluanid was > 100 mg/kg dry weight soil obtained in a seedling emergence study.

The acute study on the earthworm *Eisenia fetida* resulted in an LC_{50} > 913 mg a.s./kg d.wt. soil. A reproduction study is not available on dichlofluanid, however it has a very short persistence in soil (DT50: 1.1 days). A reproduction study with earthworms exposed to the metabolite N,N-DMS is available resulting in a NOEC of 316 mg/kg d.wt.soil. A study testing the effect of DMSA on earthworms is not available.

Soil micro-organisms exposed to dichlofluanid for 91 days showed no effects at initial concentrations of 3.41 mg a.s./kg d.wt. soil, this is therefore the NOEC. The NOEC value for soil micro-organisms (N-cycle) exposed to N,N-DMS was 17.07 mg N,N-DMS/kg d.wt. soil. A microbial test with DMSA is not available.

The effects on birds exposed to dichlofluanid are evaluated by an acute study with bobwhite quail (*Colinus virginianus*) and 5-day dietary studies with bobwhite quail and mallard duck (*Anas platyrhynchos*). In the acute study, the LD_{50} exceeded the single dose tested and the LD_{50} is therefore determined to be > 2226 mg a.s./kg bw. The LC_{50} obtained in the 5-day dietary studies could also not be determined exactly (greater than highest test concentrations) and values for both species were > 5000 mg a.s./kg feed.

PNECs

The PNEC calculations largely repeat the agreed PNECs for dichlofluanid and DMSA already determined under the PT8 review. The only major changes are the inclusion of saltwater/marine PNECs relevant to the proposed PT21 use of dichlofluanid and the inclusion of PNEC values for the metabolite N,N-DMS, data for which are also included in the dichlofluanid and tolylfluanid (CA Finland) PT 7 reviews. N,N-DMS PNEC values are in line with those used in the July 2014 CAR for tolylfluanid (PT21).

2.2.2.3. Exposure assessment

The environmental exposure assessment has been produced using all of the relevant information available in the Organisation for Economic Co-operation and Development (OECD) series on Harmonisation of Emission Scenario Documents (ESDs); '*An Emission Scenario Document for Antifouling Products in OECD countries*' (OECD, 2004) and where necessary the Technical guidance document for risk assessment (TGD; EC, 2003) and the summary of Technical Agreements for PT21 substances discussed at TMI2013. Reference has also been made to the various PT21 guidance documents developed via the TM e-consultation group.

The active substance dichlofluanid is being supported for Approval in two products:

- Alukote A (dichlofluanid only: 4.04 % w/w wet paint)
- Interspeed Ultra Variant (Copper oxide: 44.27 % w/w wet paint and dichlofluanid 2.94 % w/w wet paint).

Both of these products use dichlofluanid at concentrations typical of products used on pleasure craft and are designed for application by non-professionals. For the environmental risk assessment the highest concentration (4.04 %) has been used as a worst case scenario. The exposure and subsequent risk assessment (detailed in Document II-C) concentrates on dichlofluanid alone as the active substance for the purposes of Approval consideration. However, for product authorisation a consideration of the need for a combined risk assessment for all active substances and/or substances of concern may be necessary based on the final product composition.

There are two main scenarios where the biocides from antifouling paints could enter the environment. The first entry route is from application and removal of paints during vessel construction and routine maintenance. The second is direct release to the aquatic environment during use, where the biocides will leach directly into the aquatic environment when the vessel is in-service.

The application and removal phases of use have been developed as part of the OECD ESD project and are considered together as there are similarities in terms of location of activity, emission controls and best practices. For the aquatic assessment, a tiered approach to the assessment has been adopted where appropriate. For the calculation of predicted environmental concentrations (PECs) at tier 1 the emission loads based on the OECD ESD enter a static water body with the dimensions of the OECD-EU marina. The refinement at Tier 2 consists of simulation with the MAM-PEC model using the same emission loads

entering the OECD-EU marina. At Tier 2 the results are separated into the MAM-PEC PEC values within the marina (Tier 2a) and also the PEC values in the adjacent areas (labelled 'surrounding' in the model), taken as being representative of the wider environment (Tier 2b). All concentrations are reported as the average total concentrations predicted by MAM-PEC for simplicity.

The in-service use of the product is a principle route of entry into the environment for the active substance after it is applied to the surface of a vessel. The leaching of an active substance from a painted surface largely depends on the paint formulation and matrix type. A leaching rate can be estimated from real data (laboratory or field investigations), or predicted by modelling the total active substance content against the in-service life of the paint. Typically, the leaching of compounds from antifouling paints exhibits an exponential decay rate (i.e. high initial loss of the compound followed by an asymptotic levelling off). Antifouling paints are designed to achieve this pattern of loss in order to give a continuous steady release of biocide over the lifetime of the paint. In doing so it can be guaranteed that there will be sufficient biocide release to ensure acceptable efficacy throughout the life of the paint. For dichlofluanid the leach rate has been calculated using the CEPE mass balance method giving an estimated value of 3.91 µg dichlofluanid cm^{-2} d^{-1} (based on the product Alukote A). Kinetic input parameters were selected according to the guidance document finalised at TMIII2013. PEC values were calculated using the MAM-PEC model for the OECD-EU marina and Swiss freshwater marina scenarios. The Swiss marina is not an agreed scenario but was included to address concerns over the formation of N,N-DMS in freshwater environments. Concentrations of known metabolites have been estimated by applying the percentage reported from aerobic aquatic degradation studies with adjustment for molecular mass. Again, all concentrations are reported as the average total concentrations predicted by MAM-PEC for simplicity.

Both the principle routes of exposure have been assessed individually according to the OECD ESD as well as considering the potential for simultaneous multiple exposure based on draft guidance of the PT21 e-consultation group (i.e. considering exposure from application or removal losses combined with losses during the service life).

Where a particular Member State concern exists that is not covered by the scenarios available the UK CA recommends that a detailed consideration of this should be made at the product authorisation stage.

2.2.2.4. Risk characterisation

A summary of the risk assessment detailed in Document IIC is presented in the following sections for dichlofluanid, and the metabolites DMSA, and N,N-DMS. The risk is considered to be acceptable when PEC/PNEC < 1.

2.2.2.4.1. *Risk to the aquatic compartment (including sediment)*

Risks to local STP

Only worst case scenarios PEC / PNEC values are reported for emissions to STPs as there was an acceptable risk for all scenarios for both dichlofluanid and DMSA. No PNEC value was available for N,N-DMS.

Table 2.22 PEC:PNEC values for dichlofluanid and DMSA emissions to a local STP resulting from the use of antifouling paints (maintenance / repair of pleasure craft)

Scenario	Application or removal	Dichlofluanid (worst case)			DMSA (worst case)		
		PNEC STP (µg/L)	PEC$_{STP}$ (µg/L)	PEC / PNEC	PNEC$_{STP}$ (µg/L)	PEC$_{STP}$ (µg/L)	PEC / PNEC
Pleasure craft							
Maintenance / repair (non-professional)	Application	190	0.096	5.05E-04	11400	0.058	5.06E-06
	Removal		2.692	0.014		1.618	1.42E-04

Risks to surface water (application and removal)

A summary of the risks posed by these various routes of exposure is shown in Table 2.23 for dichlofluanid and Table 2.24 for DMSA and N,N-DMS. Only worst case scenarios at tier 1 are reported for the metabolites as risks were shown to be acceptable based on these simple tier assessments.

The use of dichlofluanid results in an unacceptable risk for the worst case direct exposure of water from the removal of anti-fouling paint from pleasure craft at tier 1. However, there was an acceptable risk at tier 2, both within and adjacent to the marina. The risk was also acceptable for indirect exposure of water via STPs for all scenarios. It should be noted that PEC/PNEC ratios for freshwater via STP are equal to those for marine water as both the freshwater PNEC and PEC values are ten times greater than the equivalent marine values.

The PNEC (aquatic species) for the degradation products DMSA and N,N-DMS are much greater than for dichlofluanid and consequently the risk was acceptable for all scenarios for DMSA and N,N-DMS.

Table 2.23 PEC:PNEC values for dichlofluanid emissions to surface water resulting from the use of antifouling paints (maintenance / repair of pleasure craft)

Scenario	Application or removal	Tier	Compart-ment	PNEC (µg/L)	Dichlofluanid			
					PEC$_{water}$ (µg/L)	PEC / PNEC	PEC$_{water}$ (µg/L)	PEC / PNEC
					Worst case		Typical case	
Maintenance / repair (non-professional)	Removal	Tier 1	Water (direct emission)	0.0064	0.067	**10.47**	-	-
		Tier 2a			5.31E-03	0.83	-	-
		Tier 2b			4.19E-05	6.55E-03	-	-
Maintenance / repair (non-professional)	Application	Tier 1	Water (via STP)	0.064	1.00E-03	1.56E-02	-	-
	Removal				0.032	0.50	4.00E-03	0.063

Table 2.24 PEC:PNEC values for DMSA and N,N-DMS emissions to surface water (worst case values) resulting from the use of antifouling paints (maintenance / repair of pleasure craft)

Scenario	Application or removal	Compart-ment	DMSA			N,N-DMS		
			PNEC (µg/L)	PEC_{water} (µg/L)	PEC / PNEC	PNEC (µg/L)	PEC_{water} (µg/L)	PEC / PNEC
Pleasure craft								
Maintenance / repair (non-professional)	Removal	Water (direct emission)	19.4	0.035	1.82E-03	1000	0.017	1.70E-05
Maintenance / repair (non-professional)	Application	Water (via STP)	194	3.40E-03	1.75E-05	10000	3.58E-03	3.58E-07
	Removal			0.095	4.92E-04		0.100	1.00E-05

Risk to surface water (in-service)

There was an unacceptable risk within both the OECD-EU marina and the Swiss marina. The risk was acceptable in the surrounding waters (Table 2.25). The risk was acceptable for all scenarios for the metabolites (Table 2.26).

Table 2.25 PEC:PNEC values for dichlofluanid emissions to surface water resulting from the use of antifouling paints (in-service uses)

Scenario	Location	Dichlofluanid		
		$PNEC_{water}$ (µg/L)	PEC_{water} (µg/L)	PEC / PNEC
OECD-EU marina	Within	0.0064	0.244	**38.13**
	Surrounding		2.32E-03	0.284
Swiss marina	Within	0.064	0.434	**6.78**
	Surrounding		3.40E-06	5.31E-05

Table 2.26 PEC:PNEC values for DMSA and N,N-DMS emissions to surface water resulting from the use of antifouling paints (in-service uses)

Scenario	Location	DMSA			N,N-DMS		
		$PNEC_{water}$ (µg/L)	PEC_{water} (µg/L)	PEC / PNEC	$PNEC_{water}$ (µg/L)	PEC_{water} (µg/L)	PEC / PNEC
OECD-EU marina	Within	19.4	0.228	1.18E-03	1000	0.112	1.12E-04
	Surrounding		1.91E-03	9.85E-05		9.44E-4	9.44E-07
Swiss marina	Within	194	7.01	3.61E-02	10000	3.46	3.46E-04
	Surrounding		8.83E-04	4.55E-06		4.37E-04	4.37E-08

Cumulative risk assessment

The in-service life stage showed an unacceptable risk assessment for dichlofluanid for the OECD-EU marina and so inevitably the cumulative risk assessment also showed an unacceptable risk at tier 2a (Table 2.27). Adjacent to the marina the risk was acceptable.

Table 2.27 Cumulative risk assessment for the OECD-EU marina

Description	$PNEC_{water}$ (µg/L)	Cumulative worst case		Cumulative typical case	
		PEC_{water} (µg/L)	PEC / PNEC	PEC_{water} (µg/L)	PEC / PNEC
OECD-EU marina (non-professional removal)					
Tier 2a (within marina)	0.0064	0.250	**39.06**	-	-
Tier 2b (adjacent to marina)		1.86E-03	0.291	-	-

Risk to sediment

The quantitative sediment risk assessment was not carried out for dichlofluanid because it was not detected in the sediment of the water / sediment study and no appropriate sediment PNEC value was available. The risk to sediment from DMSA and N,N-DMS was found to be acceptable for direct emissions. The risk to sediment from in-service uses for both metabolites was also acceptable in all cases, as was the cumulative risk from application and removal processes and in-service uses.

Summary (aquatic compartment)

The risk from maintenance and repair of pleasure craft was acceptable.

From in-service use and the cumulative risk assessment, the risks in the adjacent area (tier 2b) are considered acceptable for the purposes of active substance Approval. Tier 2b estimates concentrations in the area adjacent to the marina and this area is considered

representative of the wider environment. It has been agreed at TM level that acceptable risks in the wider environment may be used for the purposes of active substance Approval, although the risks identified within the marina environment may need to be addressed at Member State level during product authorisation.

The predicted concentrations of N,N-DMS in terms of potential precursor to N-nitrosodimethylamine) in freshwater are considered separately in Section 2.2.2.4.4.

2.2.2.4.2. *Risk to the terrestrial environment*

Risks to the soil compartment

The risks to the soil environment from dichlofluanid (Table 2.28) following direct emission (worst case) were acceptable for application but unacceptable for removal (both worst and typical case). The risk was also unacceptable for the single application and removal (maintenance) cycle. The risk from the metabolite DMSA (Table 2.29) was acceptable for application but was unacceptable for removal (worst case) and for a single application and removal cycle (worst and typical case). The risk was acceptable for removal (typical case). There was an acceptable risk for the application and removal scenarios for N,N-DMS (Table 2.30). The risk from the maintenance cycle was unacceptable (worst and typical cases).

Risks from indirect emissions to soil via sewage sludge application were acceptable for dichlofluanid; the metabolites are not predicted to occur in sewage sludge.

Table 2.28 PEC:PNEC values (worst case) for dichlofluanid emissions to soil resulting from the use of antifouling paints (maintenance / repair of pleasure craft)

Scenario	Application or removal	Environmental compartment	$PNEC_{soil}$ (mg kg^{-1})	Dichlofluanid (worst case)		Dichlofluanid (typical case)	
				PEC_{soil} (mg kg^{-1})	PEC / PNEC	PEC_{soil} (mg kg^{-1})	PEC / PNEC
Pleasure craft							
Maintenance / repair (non-professional)	Application	Direct to soil (from average emission rate)	0.039	0.030	0.77	-	-
	Removal			0.837	**21.46**	0.108	**2.77**
Maintenance / repair (non-professional)	Application	Indirectly to soil in sewage sludge (from average emission rate)	0.039	2.70E-05	6.92E-04	-	-
	Removal			7.56E-04	1.94E-02	9.72E-05	1.47E-03
Maintenance / repair (non-professional)	Application and removal	Direct to soil (five maintenance cycles)	0.039	0.762	**19.54**	2.504	**64.2**

Table 2.29 PEC:PNEC values (worst case) for DMSA emissions to soil resulting from the use of antifouling paints (maintenance / repair of pleasure craft)

Scenario	Application or removal	Environmental compartment	$PNEC_{soil}$ (mg kg^{-1})	DMSA (worst case)		DMSA (typical case)	
				PEC_{soil} (mg kg^{-1})	PEC / PNEC	PEC_{soil} (mg kg^{-1})	PEC / PNEC
Pleasure craft							
Maintenance / repair (non-professional)	Application	Direct to soil (from average emission rate)	0.242	0.018	0.07	-	-
	Removal			0.503	**2.08**	0.065	0.27
Maintenance / repair (non-professional)	Application and removal	Direct to soil (five maintenance cycles)	0.242	2.031	**8.39**	6.674	**171.1**

Table 2.30 PEC:PNEC values (worst case) for N,N-DMS emissions to soil resulting from the use of antifouling paints (maintenance / repair of pleasure craft)

Scenario	Application or removal	Environmental compartment	$PNEC_{soil}$ (mg kg^{-1})	N,N-DMS (worst case)		N,N-DMS (typical case)	
				PEC_{soil} (mg kg^{-1})	PEC / PNEC	PEC_{soil} (mg kg^{-1})	PEC / PNEC
Pleasure craft							
Maintenance / repair (non-professional)	Application	Direct to soil (from average emission rate)	0.339	2.56E-03	0.01	-	-
	Removal			0.072	0.21	9.22E-03	0.03
Maintenance / repair (non-professional)	Application and removal	Direct to soil (five maintenance cycles)	0.339	0.295	0.87	0.970	**2.86**

The risks to the soil environment may be mitigated by use of appropriate label phrases to reduce the exposure. The use of risk mitigation for non-professional users of PT21 products has not been agreed at WG or CA level. However it is possible that limited forms of mitigation, such as advising users to protect the soil environment during application and removal activities, may be considered acceptable.

Risks to groundwater

Low risk to groundwater is expected from direct exposure to the soil based on the likely limited areas of soil exposure. There is the potential for exposure of a wider area after indirect exposure after application of sewage sludge therefore $PEClocal_{soil,\ porewater}$ values were calculated for dichlofluanid, DMSA, and N,N-DMS only for the indirect exposure route (Table 2.31). For all three substances PEC values in the pore water are below the trigger value (0.10 $\mu g L^{-1}$) for the typical case and therefore the risk to groundwater is acceptable.
The predicted concentrations of N,N-DMS in terms of potential precursor to N-nitrosodimethylamine) in freshwater are considered separately in Section 2.2.2.4.4.

Table 2.31 Summary of PEClocal$_{soil, porewater}$ values (indirect emission route) for pleasure craft

Scenario	Application or removal	PEClocal$_{soil, porewater}$ (µg L^{-1})					
		Dichlofluanid		DMSA		N,N-DMS	
		Worst	Typical	Worst	Typical	Worst	Typical
Pleasure craft							
Maintenance / repair (non-professional)	Application	0.001	-	0.014	-	0.017	-
	Removal	0.028	0.004	0.382	4.91E-02	0.487	0.063

2.2.2.4.3. *Risks to the atmosphere*

Negligible exposure of the atmosphere is predicted for dichlofluanid or DMSA based on their physicochemical properties.

2.2.2.4.4. *N, N-DMS as a precursor of NDMA*

A summary of maximum PEClocalwater values for N,N-DMS is presented in Table 2.32. Although no unacceptable risk was identified for N,N-DMS in surface water, it is a potential precursor to N-nitrosodimethylamine (NDMA) during ozonation as part of water treatment. For this reason it was agreed at TMI08 that the drinking water limit value of 0.10 µg/L should be used in the risk assessment of N,N-DMS. On this basis the risk is acceptable in surface water from direct emission, but unacceptable from indirect emission via STPs. The risk is acceptable in groundwater.

The PEC$_{water}$ value from in-service use in freshwater was 3.46 µg/L. Monitoring in the Netherlands (reported as part of the submission of tolylfluanid) found concentrations of N,N-DMS between 0.29 and 2.25 µg/L in recreational lakes. Concentrations > 0.10 µg/L were also reported in a separate monitoring study of surface water used for production of drinking water.

Table 2.32 Summary of maximum PEClocal$_{water}$ values for N,N-DMS from the different emission routes to water

Scenario	Emission route to water	PEC$_{water}$ (µg/L)
		N, N-DMS
Maintenance and repair (non-professional removal)	Surface water (direct)	0.017
Maintenance and repair (non-professional removal)	Surface water (indirect via STP)	0.100
Maintenance and repair (non-professional removal)	Groundwater (via sludge application to soil)	0.487 (worst) 0.063 (typical)

Swiss marina	Surface water (direct from in-service use)	3.46

It could be argued that surface water where there is a relatively high boat density and low water exchange rate (such as the Swiss marina scenario) is unlikely to be used as a source of drinking water. However both modelling and monitoring data indicate concentrations of N,N-DMS could exceed 0.10 µg/L and based on the agreement reached at TMI08, the risk is unacceptable for freshwater in-service use.

2.2.2.4.5. *Risks of secondary poisoning*

The risk from secondary poisoning was considered for dichlofluanid but was not necessary for the metabolites DMSA and N,N-DMS due to low accumulation potential. PEC/ PNEC values for oral predators are presented in Tables 2.33 and 2.34 for dichlofluanid, based on $PEC_{oral\ predator}$ values calculated in Doc IIA and the $PNEC_{oral\ predator}$ for dichlofluanid, which is 1.67 mg/kg.

For the consumption of fish there was an acceptable risk from both scenarios considered. The risk was unacceptable for the consumption of earthworms for direct exposure but was acceptable for indirect exposure.

Table 2.33 PEC/PNEC values for oral predators (fish)

Scenario	$PEC_{surface\ water}$ (mg L^{-1})	$PEC_{oral\ predator}$ (mg $kg_{wet\ fish}^{-1}$)	PEC / PNEC
Marina	1.26×10^{-4}	9.07×10^{-3}	5.43×10^{-3}
Swiss marina	2.17×10^{-4}	1.56×10^{-2}	9.34×10^{-3}

Table 2.34 PEC/PNEC values for oral predators (earthworms)

Scenario	Type of exposure	Worst / typical case	$PEC_{oral\ predator}$ ($C_{earthworm}$) (mg kg_{ww}^{-1})	PEC / PNEC
Maintenance / repair (non-professional) removal / application cycle	direct	worst	3.92	**2.35**
Maintenance and repair (non-professional) removal	indirect	worst	1.18E-03	7.07E-04

2.2.2.5. PBT and POP assessment

PBT assessment

Under the Biocidal Products Regulation (BPR), a PBT assessment is needed to demonstrate that a substance does not fulfil selection criteria under the United Nations Environment Programme – Persistent Organic Pollutants convention (UNEP-POPs) to limit emissions to the environment of those chemicals with high potential for persistence, bioaccumulation,

long range transport and adverse effects on human health and the environment. Any active substance which is found to be either a PBT or very Persistent very Bioaccumulative (vPvB) substance shall not be Approved unless releases to the environment can be effectively prevented.

Persistence

The criteria for persistence according to Commission regulation 253/2011:

- The degradation half-life in marine water is higher than 60 days, or
- the degradation half-life in fresh or estuarine water is higher than 40 days, or
- the degradation half-life in marine sediment is higher than 180 days, or
- the degradation half-life in fresh or estuarine water sediment is higher than 120 days, or
- the half-life in soil is higher than 120 days.

Dichlofluanid was shown to be hydrolytically unstable at all environmentally relevant pH and temperatures. Absorption of light was low and dichlofluanid was therefore assumed to be stable to photolysis. Significant degradation occurred in a prolonged Closed Bottle ready biodegradation test and it was classified as inherently biodegradable. Dichlofluanid was degraded rapidly in the water / sediment system (DT_{50} for the whole system < 1 day) and in soil (DT_{50} < 1 day). The UK CA concludes that dichlofluanid will not breach any persistence triggers. The metabolite DMSA has a dissipation DT_{50} in freshwater of 189.0 days and N,N-DMS > 1 year therefore both fulfil the persistent criteria set out above and also the very persistent criteria (stated in Annex XIII as the half-life in water is greater than 60 days). The triggers are breached even without temperature correction to environmental conditions. The aerobic soil DT_{50} value for DMSA varies from 136 to 227 days at 12°C (derived from the range 58 to 97 days at a study temperature of 23°C using a Q_{10} of 2.2).

In conclusion, dichlofluanid will not breach any persistence triggers. However the metabolites DMSA and N,N-DMS fulfil both the persistent criteria and the very persistent criteria.

Bioaccumulation

Dichlofluanid has a log Kow < 4.5 and therefore bioaccumulation potential is not indicated. Also its half-life in water is less than 12 hours and this mitigating property also suggests that no accumulation is likely. The bioaccumulation study showed rapid accumulation and depuration of dichlofluanid in / from bluegill sunfish with a total residue BCF of 72 and it can be concluded that dichlofluanid will not tend to accumulate. DMSA and N,N-DMS both have log Kow values < 4.5 therefore no indication of accumulation potential.

In conclusion, bioaccumulation potential is not indicated for dichlofluanid, DMSA or N,N-DMS.

Toxic

A substance is considered to fulfil the toxicity criterion when the long-term NOEC for marine or freshwater organisms is less than 0.01 mg l^{-1} (Commission regulation 253/2011). The chronic *Skeletonema costatum* NOEC for dichlofluanid is 0.00064 mg a.s. l^{-1}. A substance is also considered to be potentially toxic when the L(E)C50 to aquatic organisms is less than 0.1 mg l^{-1}. The dichlofluanid LC50 for rainbow trout is 0.01 mg a.s. l^{-1}. The toxic criterion is therefore triggered for dichlofluanid.

The lowest chronic NOEC from studies with the metabolite DMSA was the 21 d NOEC = 10 mg l^{-1} for rainbow trout, while the lowest L(E)C50 from the available acute studies was > 95.6 mg l^{-1} for *Daphnia magna*. The toxic criterion is therefore not triggered for DMSA.

The chronic NOECs from studies with the metabolite N,N-DMS were the 28 d NOEC = 100 mg a.s. l^{-1} for rainbow trout and the 21 d NOEC for *Daphnia magna* = 100 mg a.s. l^{-1}. All L(E)C50 values from the available acute studies were > 100 mg l^{-1}. The toxic criterion is therefore not triggered for N,N-DMS.

In conclusion, the toxic criterion is triggered for dichlofluanid but not for DMSA or N,N-DMS.

PBT Conclusion

Dichlofluanid does not breach the persistent or bioaccumulation criteria therefore it can be concluded that it is not a PBT substance. Dichlofluanid also does not breach the criteria of a vPvB substance. DMSA breaches the persistent and very persistent criteria but not the bioaccumulative or toxic criteria therefore it is not considered to be a PBT substance. Similarly N,N-DMS only breaches the persistent and very persistent criteria therefore is also not a PBT substance.

POP assessment

The criteria for a substance being a persistent organic pollutant (POP) are 'P', 'B' and having the potential for long range transport. In addition, high toxicity can breach the 'B' criterion, in which case a substance will be a persistent organic pollutant if it is 'P', demonstrates the potential for long range transport, and is either 'B' or 'T'.

Dichlofluanid is not persistent and therefore does not fit the criteria for being a POP. DMSA and N,N-DMS are both very persistent but neither are bioaccumulative or toxic criteria and so do not fit the criteria for being a POP.

2.2.3. Assessment of endocrine disruptor properties

There were no significant effects relevant to humans on endocrine organs and/or reproduction in standard mammalian toxicity studies. Thyroid toxicity, seen at high doses also producing a range of other toxicities, was by a mode of action (thyroid peroxidase inhibition) considered by EU experts (ECB, 1999) to be not relevant to humans. Instances of testicular degeneration were noted in the 1-year study in beagle dogs, at 37.5 mg/kg/day a dose that produced body weight deficits. In contrast, increased interstitial tissue, but not testicular degeneration was reported at doses of up to 34 mg/kg/day in a longer dog study of two years. No testicular toxicity was observed in repeated dose studies in rats and mice. It was also noted that no effects on fertility were observed in rat multigeneration studies at doses of up to 590-780 mg/kg/day. Adrenal zona fasciculata vacuolation was seen in the 2 year dog study only at a dose level also producing poor condition and body weight deficits. It is therefore concluded that dichlofluanid does not have specific endocrine-disrupting properties relevant to a human health risk assessment. In addition, the available toxicity data do not support classification of dichlofluanid in category 2 for reproductive toxicity and category 2 for carcinogenicity (CLP). Therefore, the interim criteria for endocrine disruptors are not met.

Ecotoxicology

In the absence of a fish full life cycle study or suitable data on other organism groups, the necessary relevant information is not available to conclude on the potential for endocrine effects in wildlife. Additionally, no agreed approach exists for assessing endocrine disrupting chemicals in the environment. In the absence of guidance in assessing environmentally relevant endocrine disrupting chemicals the BRP Regulation (EU) 528/2012 states in article 5 paragraph 3:

> "Pending the adoption of those criteria, 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, shall be considered as having endocrine-disrupting properties.
>
> 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, may be considered as having endocrine-disrupting properties"

Therefore if endocrine disrupting properties are identified by the human health assessment then dichlofluanid should also be considered to possess endocrine disrupting properties from an environmental perspective. No further consideration is presented here and no studies have been submitted regarding endocrine disruption in an environmental context.

During the current assessment dichlofluanid has not been identified as an endocrine disruptor in the human health assessment. Therefore, dichlofluanid is not considered an endocrine disruptor from an environmental perspective.

2.3. Overall conclusions

The outcome of the assessment for dichlofluanid product-type 21 is specified in the BPC opinion following discussions at the seventeenth meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA web-site.

2.4. List of endpoints

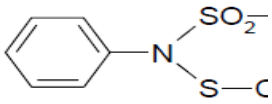
The most important endpoints, as identified during the evaluation process, are listed in Appendix I.

Appendix I: List of endpoints

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

Active substance (ISO Common Name)	Dichlofluanid
Product-type	Product type 21 (antifouling products)
Applicant	Lanxess Deutschland GmbH

Identity

Chemical name (IUPAC)	N-(Dichlorofluoromethylthio)-N',N'-dimethyl-N-phenylsulfamide
Chemical name (CA)	Methanesulfenamide, 1,1-dichloro-N-[(dimethylamino)sulfonyl]-1-fluoro-N-phenyl-
CAS No	1085-98-9
EC No	214-118-7
Other substance No.	CIPAC No 74
Minimum purity of the active substance as manufactured (g/kg or g/l)	960 g/kg
Identity of relevant impurities and additives in the active substance as manufactured (g/kg)	The identity and concentrations of the impurities in dichlofluanid, and the additives are confidential. This information is provided in the 'Confidential Annex' document.
Substances of concern	No substances of concern have been identified by the UK CA
Molecular formula	$C_9H_{11}Cl_2FN_2O_2S_2$
Molecular mass	333.2
Structural formula	

Physical and chemical properties

Melting point (state purity)	103.2 °C at the beginning of melting, 104 °C at final stage of melting (purity: 99.4%)
Boiling point (state purity)	Not measurable, substance decomposes and is not distillable
Temperature of decomposition	DTA: endothermic effect (melting) < 150 °C, no exothermic effect (decomposition); TGA: weight loss due to evaporation, sublimation and transition to decomposition, commencing at 120 °C. Dichlofluanid may be considered stable at room temperature
Appearance (state purity)	At 20 °C and 101.3 kPa: Physical state: solid powder Colour: white to slightly yellow Odour: characteristic smell, musty
Relative density (state purity)	1.575 at 20 °C (purity: 96%)
Surface tension	72.75 mN/m; not surface active (test solution concentration was 1.17 mg/l)
Vapour pressure (in Pa, state temperature)	2.15×10^{-5} Pa at 20 °C 5.37×10^{-5} Pa at 25 °C 3.03×10^{-3} Pa at 50 °C
Henry's law constant (Pa m^3 mol^{-1})	4.5×10^{-3} Pa .m^3.mol^{-1}
Solubility in water (g/l or mg/l, state temperature)	pH 4: 0.92 mg/l at 10 °C 1.58 mg/l at 20 °C 2.69 mg/l at 30 °C The solubility in water is independent of pH in the range of pH 4 to pH 9. However it hydrolyses in water especially at higher pHs.
Solubility in organic solvents (in g/l or mg/l, state temperature)	Results at 20 ºC: Xylene: 81.2 g/l Shellsol D60: 2.54 g/l Di(propylene glycol)methyl ether: 86.4 g/l 2-Methyl-2,4-pentanediol: 20.7 g/l Due to the decomposition of dichlofluanid in 1-methyl-2-pyrrolidone, the solubility in this solvent cannot be determined
Stability in organic solvents used in biocidal products including relevant breakdown products	Dichlofluanid, in a representative solvent-based paint, is stable for 8 weeks at 40 °C.
Partition coefficient (log P_{OW}) (state temperature)	log P_{ow} = 3.5 The partition coefficient was determined to be independent of temperature in the range of 10 °C to 30 °C and to be independent of pH in the range pH 4 to pH 9
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH 4, 30ºC: DT_{50} = 6.9 d pH 4, 40ºC: DT_{50} = 2.8 d

	pH 7, 20ºC: DT_{50} = 25.6 h pH 7, 30ºC: DT_{50} = 5.4 h
Dissociation constant	Dichlofluanid has no acidic or basic properties in water in the range pH 4 to pH 9
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Spectra confirms the chemical structure
Photostability (DT_{50}) (aqueous, sunlight, state pH)	Due to its lack of UV absorbance at the wavelengths present in sunlight, dichlofluanid is not degradable by direct photodegradation in aqueous solution. Even under the assumption of a quantum yield of 1, assessments of the environmental half-life by means of computer models would yield values of several years.
Quantum yield of direct phototransformation in water at Σ > 290 nm	See above
Flammability	Dichlofluanid (tested as Preventol A 4-S – 90% technical dichlofluanid plus 6% silicon dioxide 1% magnesium oxide and 3% mineral oil) is not highly flammable according to EC Test Method A.10. It does not liberate gases in hazardous amounts upon contact with water. It shows spontaneous combustion behaviour. The relative spontaneous ignition temperature is 370 °C
Explosive properties	From the chemical structure of dichlofluanid it can be concluded that dichlofluanid is not explosive
Oxidising properties	From the chemical structure it is seen that dichlofluanid will not react exothermally with flammable materials. Therefore dichlofluanid does not exhibit any oxidizing properties
Reactivity towards container material	Based on information from experience of packaging dichlofluanid and its chemical structure, the recommended container materials for direct contact with dichlofluanid are: Polypropylene plastic material (PP), High and low density Polyethylene plastic materials (HDPE, LDPE). Product package in steel drums lined with epoxy-phenolic resin.

Classification and proposed labelling

with regard to physical/chemical data	None
with regard to toxicological data	Skin Sens 1; H317 – May cause an allergic skin reaction Eye Irrit 2; H319 – Causes serious eye

	irritation Acute Tox 4; H332 – Harmful if inhaled
with regard to fate and behaviour data	None
with regard to ecotoxicological data	Aquatic Acute 1; H400 – Very toxic to aquatic life

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) Impurities in technical active substance (principle of method)	High Performance Liquid Chromatography, using UV detection, for the analysis of dichlofluanid and impurities in the active substance and formulated product. The methods were suitably validated.

Analytical methods for residues

Soil (principle of method and LOQ)	**Residue definition**: Dichlofluanid and DMSA Gas Chromatography, using Mass Selective Detection, for the analysis of dichlofluanid and DMSA in soil and sediment. The method was suitably validated. Limit of quantification (LOQ): 0.01 mg/kg for soil and sediment. **NO(A)EC**: 3.9 mg a.s./kg soil dw (soil micro-organisms)
Air (principle of method and LOQ)	**Residue definition**: Dichlofluanid Gas Chromatography, using nitrogen and phosphorous selective detection, for the analysis of dichlofluanid in air. The method was suitably validated. Limit of quantification: 0.003 mg a.s. /m^3 air **LOQ required based on AOEL** = 0.0075 mg as/m^3 air
Water (principle of method and LOQ)	**Residue definition**: Dichlofluanid and DMSA Gas Chromatography, using Electron Capture Detection, for the analysis of dichlofluanid in drinking and surface water. The method was suitably validated. Limit of quantification (LOQ): 0.1 µg/l. Gas Chromatography, using Mass Selective Detection, for the analysis of DMSA in drinking and surface water. The method was suitably validated. Limit of quantification (LOQ): 0.1 µg/l Gas Chromatography, using Mass Selective Detection, for the analysis of dichlofluanid and DMSA in sea water. The method was suitably validated. Limit of quantification

	(LOQ): 0.01 µg/l. Dichlofluanid NOEC in surface water = 2.65 µg a.s./L (*Daphnia magna*) DMSA NOEC in surface water = 9.7 mg/L (*Chironomus riparius*)
Body fluids and tissues (principle of method and LOQ)	Relevant when an active substance is classified as toxic or highly toxic. Dichlofluanid is classified as harmful (Xn) and so no analytical methods needed to be submitted.
Food/feed of plant and animal origin (principle of method and LOQ for methods for monitoring purposes)	The Applicant has not submitted analytical methods, due to dichlofluanid not being used to treat food or feeding stuffs and dichlofluanid residues do not accumulate in fish and shellfish.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Rat: ^{14}C ring labelled dichlofluanid: ≥ 90 % absorption, with maximum concentration in blood plasma within 3.0 hours 100% oral absorption is used in the risk assessments
	Rat: ^{14}C labelled fluorodichloromethyl sulphenyl group: 70 – 80 % absorption with maximum relative concentration in blood plasma within 1.5 hours
Rate and extent of dermal absorption:	12% based on a human 8/24h in vitro study with a formulated product.
Rate and extent of inhalation absorption	100% default value - no data available.
Distribution:	Widely distributed with generally low concentrations, except for liver, kidney, thyroid and erythrocytes.
Potential for accumulation:	None. Dichlofluanid was found to not accumulate in the carcass or carcass minus gastrointestinal tract.
Rate and extent of excretion:	≥ 99% during the first 48 hours after oral application; mainly via urine, but also via faeces and the breath.
Toxicologically significant metabolite(s)	Parent compound, fluoride ion

Acute toxicity

Rat LD_{50} oral	> 5000 mg/kg (males + females)
Rat LD_{50} dermal	> 2000 mg/kg (males + females)
Rat LC_{50} inhalation	About 1200 mg/m^3/4 h (males + females) *(sic PT8)*
Skin irritation	Not classified for this effect.
Eye irritation	Irritating to eyes
Skin sensitization (test method used and result)	Sensitising (Magnusson-Kligman test)

Repeated dose toxicity

Species/ target / critical effect	Dogs – liver (disturbance of liver function and hepatic cell damage), kidney (nephropathy and disturbance of kidney function), thyroid (reduction of thyroid hormones)
Lowest relevant oral NOAEL / LOAEL	2.5 mg/kg/day (chronic dog)
Lowest relevant dermal NOAEL / LOAEL	28 day rat (22 exposures; 6h/d) Systemic >1000 mg/kg bw/d

	Local irritation <100 mg/kg bw/d
Lowest relevant inhalation NOAEL / LOAEL	No data

Genotoxicity

	Dichlofluanid was found to be a point mutagen in studies on bacteria and in the mouse lymphoma strain L5178Y at cytotoxic concentrations. Further *in vitro* tests on point mutations on the HPRT locus in eukaryotic cells yielded negative results. The available data indicate that dichlofluanid was not an *in vivo* somatic or germ cell mutagen.

Carcinogenicity

Species/type of tumour	Thyroid tumour incidences were increased at the top dose level in male and female rats. Single incidences were seen at lower doses. Threshold mode of action supported. Overall, dichlofluanid is a low potency, non-genotoxic carcinogen, causing thyroid tumours in rats by inhibition of TPO activity. Taking account of the conclusions of the Specialised Experts on carcinogenicity, the mechanism of toxicity is not relevant to humans and classification for carcinogenicity is not justified.
lowest dose with tumours	4500 ppm (equal to 300 – 420 mg/kg bw/day)

Reproductive toxicity

Species/ Reproduction target / critical effect	Rat: Pups – reduced weights, elevated liver and kidney weights
Lowest relevant reproductive NOAEL / LOAEL	NOAEL (parental) of 180 ppm equiv. to 16/21 mg/kg/day (m/f)
Species/Developmental target / critical effect	No compound related effects on development
Lowest relevant developmental NOAEL / LOAEL	NOAEL of 30 mg/kg/day *(Rabbits;maternal toxicity*)

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	No indications for special concern

Other toxicological studies

....	No indications for special concern

Medical data

....	No indications for special concern. A few cases of allergic skin reactions are described among manufacturing plant personnel.

Summary	Value	Study	Safety factor
Non-professional user			
ADI (acceptable daily intake, external long-term reference dose) [CHANGED FROM PT8]	0.025 mg/kg/day	Dog 1 year	100
AEL-acute (Operator Exposure)	0.3 mg/kg/day	Rabbit developmental	100
AEL-medium term (Operator Exposure)	0.025 mg/kg/day	Dog 1 year	100
AEL-long-term (Operator Exposure)	0.025 mg/kg/day	Dog 1 year	100
ARfD (acute reference dose) [CHANGED FROM PT8]	0.3 mg/kg bw	Rabbit development.	100.
Professional user			
AEL-acute (Operator Exposure)	0.3 mg/kg/day	Rabbit developmental	100
AEL-medium term (Operator Exposure)	0.025 mg/kg/day	Dog 1 year	100
AEL-long-term (Operator Exposure)	0.025 mg/kg/day	Dog 1 year	100
Reference value for inhalation (proposed OEL)	Not derived		
Reference value for dermal absorption concerning the active substance	12%	Human in vitro with Interspeed Ultra Variant.	N/A
Reference value for dermal absorption concerning the representative product(s)	Not derived	Further information required for product authorisation once specific guidance on PT21 available	N/A

Acceptable exposure scenarios (including method of calculation)

Products:-
'Alukote A' (4.04% w/w dichlofluanid)
Interspeed Ultra Variant' (2.94% w/w dichlofluanid)

Exposure routes:
Direct exposure – dermal and inhalation
Indirect exposure – dermal and oral

Systemic acute AEL for all exposures = 0.3 mg/kg bw/day

Method of calculation: AEL approach

Professional users	Non requested – not applicable
Production of active substance:	Not applicable
Formulation of biocidal product	Not applicable
Non-professional users	Application by brush and roller to small pleasure craft. Cleaning of brushes Removal of old paint from hulls
Indirect exposure as a result of use	Laundering of work clothes Contact with wet or dry paint Dietary exposure

Direct exposures

Task	Estimated uptake mg/kg bw/d	Estimated exposure as % AEL
Brush and roller application. Wearing gloves and normal clothes.	Alukote A - Tier 4	82
	Interspeed Ultra Variant – Tier 4	60
Cleaning paint brushes	Alukote A - Tier 1	5
	Interspeed Ultra Variant – Tier 1	4
Paint removal (high pressure washing or abrasion) Wearing gloves and normal clothes	Alukote A Tier 4	5
	Interspeed Ultra Variant – Tier 4	3

Indirect exposures

Task	Estimated uptake mg/kg bw/d	Estimated exposure as % AEL
Adult laundering contaminated work clothes	Alukote A - Tier 1	9
	Interspeed Ultra Variant – Tier 1	6
Young child touching wet paint from a boat surface	Alukote A - Tier 1	473*
	Interspeed Ultra Variant – Tier 1	406*
Young child touching dry paint from a boat surface	Alukote A Tier 4	45
	Interspeed Ultra Variant – Tier 4	32

*It is considered that such risks could be mitigated by an additional warning on the product label, namely:
'KEEP UNPROTECTED PERSONS AND ANIMALS AWAY UNTIL TREATED SURFACES ARE DRY'

Indirect exposure via food.

Systemic effects from exposure from the consumption of food are unlikely. Based on the highest PEC, predicted exposures from marine fish are very low, with the ADI not being exceeded even by the consumption of 1 kg fish per kg bw/day. The risks from oral exposures are considered acceptable.

Combined exposures

The following scenarios were considered: application of new paint and cleaning of brushes. Risks are considered acceptable.

Combined systemic exposures to dichlofluanid arising from 'Alukote A' and 'Interspeed Ultra Variant' are below the acute AEL if gloves and normal clothing are worn during the brush / roller application of new material. These are considered to be reasonable expectations for the activities involved.

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)	**Freshwater** Dichlofluanid pH 7, 20°C: DT_{50} = 25.6 h pH 7, 30°C: DT_{50} = 5.4 h pH 4, 30°C: DT_{50} = 6.9 d pH 4, 40°C: DT_{50} = 2.8 d DMSA pH 4, 7, and 9; 55°C; no degradation after 7 days N, N-DMS pH 4, 7, and 9; 50°C; no degradation after > 10 days **Seawater** Dichlofluanid pH 8.2, 10°C: DT_{50} = 3.3 h pH 8.2, 20°C: DT_{50} = 1.2 h pH 8.2, 30°C: DT_{50} = 0.8 h
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Dichlofluanid DT_{50} > 1 year
Readily biodegradable (yes/no)	Dichlofluanid: No; 9% after 28 d DMSA: No; 6% after 28 d
Biodegradation in seawater	No information provided
Distribution in water / sediment systems (active substance)	**Freshwater only** Geomean DT_{50} = 0.09 d (20.5°C) Geomean DT_{50} = 0.18 d (12°C) **Freshwater/sediment system** Aqueous phase: geomean DT_{50}= 0.07 d (20.5°C) Aqueous phase: geomean DT_{50}= 0.17 d (9°C) Whole system : geomean DT_{50}= 0.12 d (20.5°C) Whole system : geomean DT_{50}= 0.30 d (9°C) **% ^{14}C- recovery at end of test:** < 0.1% AR (water) < 0.1% AR (sediment) < 0.1% AR (system)
Distribution in water / sediment systems (metabolites)	**Freshwater/sediment system** DMSA Aqueous phase: geomean DT_{50} = 189.0 d (20.5°C) Aqueous phase: geomean DT_{50} = 467 d

	(9°C) Whole system : geomean DT_{50} = 187.9 d (20.5°C) Whole system : geomean DT_{50} = 464 d (9°C) **% AR at end of test (120 d):** 63.2% and 53.6% (water) 7.7% and 4.4% (sediment) 70.9% and 58.0% (system) <u>N, N-DMS</u> Aqueous phase: geomean DT_{50} > 1 year (20°C) Whole system : geomean DT_{50} > 1 year (20°C) **% AR at end of test (120 d):** 66.4% and 46.1% (water) 9.6% and 14.9% (sediment) 76.0% and 61.0% (system)
Mineralization	3.3% AR and 5.1% AR (after 120 days)
Non-extractable residues	17.6% AR and 19.0% AR (after 120 days)

Route and rate of degradation in soil	
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (23°C, aerobic): < 1 day (dichlofluanid) DT_{50lab} (23°C, aerobic): 58 to 97 days (DMSA); 136 to 227 days at 12°C
	DT_{90lab} (20°C, aerobic): not calculated
	DT_{50lab} (10°C, aerobic): no information provided
	DT_{50lab} (20°C, anaerobic): no information provided
	Degradation in the saturated zone: no information provided
Mineralization (aerobic)	9.2 to 22.6% AR
Non-extractable residues	56.0 to 75.7% AR
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	DMSA (maximum 79.5 to 84.0% AR at day 1; 1.4 to 17.8% AR at the end of study) N,N-DMS (23.1% AR); bridged from tolylfluanid
Field studies (state location, range or median with number of measurements)	No information provided
Anaerobic degradation	Rapid degradation to DMSA (87.4 to 95.5% after 30 days)
Soil photolysis	No information provided
Non-extractable residues	No information provided

Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	No information provided
Soil accumulation and plateau concentration	No accumulation potential
Laboratory studies (range or median, with number of measurements, with regression coefficient)	No accumulation study reported

Adsorption/desorption	
Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	Ka_{oc} (dichlofluanid): 1344 mL/g Ka_{oc} (DMSA): 53 mL/g pH dependence: no

Fate and behaviour in air

Direct photolysis in air	No information provided
Quantum yield of direct photolysis	No information provided
Photo-oxidative degradation in air	Half-life = 25.8 h assuming a 24 h day and OH radical concentration of 5×10^5 OH/cm^3
Volatilization	No information provided but assumed to be low based on vapour pressure of 2.15×10^{-5} Pa at 20 °C

Monitoring data, if available	
Soil (indicate location and type of study)	None
Surface water (indicate location and type of study)	Dedicated study (Greece, marinas)
Ground water (indicate location and type of study)	None
Air (indicate location and type of study)	None

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Salmo gairdneri (now *Oncorhynchus mykiss)*	96 hours	Mortality	LC_{50} = 0.01 mg/l NOEC < 0.0026 mg/l
Salmo gairdneri (now *Oncorhynchus mykiss)*	21 days	Mortality and symptoms	NOEC = 0.00455 mg/l
Pimephales promelas	33 days	Mortality and symptoms	NOEC = 0.00407 mg/l
Invertebrates			
Daphnia magna	48 hours	Immobility	EC_{50} = 0.42 mg/l
Daphnia magna	21 days	Immobility, reproduction	NOEC = 0.00265 mg/l
Algae			
Scenedesmus subspicatus	72 hours	Growth inhibition	E_bC_{50} = 10.8 mg/l E_rC_{50} = 15 mg/l NOEC = 1.0 mg/l
Skeletonema costatum (marine diatom)	72 hours	Growth inhibition	NOEC = 0.00064 mg/l
Aquatic micro-organisms			
Activated sludge	3 hours	Inhibition of respiratory rate	EC_{50} = 19 mg/l (remark: water solubility of dichlofluanid is 1.3 mg/l)

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	21 days	Mortality Body weight and length	LC_{50} > 100 mg/l NOEC = 10 mg/l
Invertebrates			
Daphnia magna	48 hours	Immobility	EC_{50} > 95.6 mg/l
Chironomus riparius (sediment-dweller)	28 days	Development	EC_5 = 9.7 mg/l
Algae			
Scenedesmus subspicatus	72 hours	Growth inhibition	EC_{50} > 97.7 mg/l NOEC = 9.7 mg/l
Aquatic micro-organisms			

Activated sludge	30 mins	Inhibition of respiratory rate	EC_{50} = 1140 mg/l

Toxicity data for aquatic species (most sensitive species of each group)
METABOLITE: N,N-DMS

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	96 hours	Mortality	LC_{50} > 100 mg/l
Oncorhynchus mykiss	28 days	Mortality, symptoms	NOEC = 100 mg/l
Invertebrates			
Daphnia magna	48 hours	Immobility	EC_{50} > 100 mg/l
Daphnia magna	21 days	Immobility, reproduction	NOEC = 100 mg/l
Algae			
Scenedesmus subspicatus	72 hours	Growth inhibition	EC_{50} > 100 mg/l NOEC = 100 mg/l
Aquatic micro-organisms			
Not available			

Effects on earthworms or other soil non-target organisms

Acute toxicity to earthworms: dichlofluanid (tested as 51.3% w/w WG form.n)	*Eisenia fetida*: LC_{50} (14 days) = > 913 mg a.s./kg d.wt soil
Chronic toxicity to earthworms: only metabolite N,N-DMS tested	*Eisenia fetida:* *NOEC (56 days) = 316 mg/kg d.wt soil*

Effects on soil micro-organisms

Nitrogen mineralization Carbon mineralization	Dichlofluanid does not cause adverse effects to the soil carbon and nitrogen cycle at the concentration of 3.41 mg a.s./kg dwt soil. A dose of 34.1 mg a.s./kg dwt soil caused a temporary reduction in the amount of glucose degraded. This dose also induced a temporary inhibition and, subsequently, a temporary stimulation of nitrogen mineralisation in both soils. 3.41 mg a.s./kg dwt soil is used as a NOEC.
Nitrogen mineralization Carbon mineralization	N,N-DMS did not cause effects on soil micro-organisms (N-cycle) at concentrations of 17.07 mg N,N-DMS/kg d.wt. soil. This value can be considered the NOEC.

Effects on terrestrial vertebrates

Acute toxicity to birds	*Colinus virginianus*: LD_{50} > 2226 mg/kg bw
Sub-acute toxicity to birds	*Colinus virginianus* and *Anas platyrhynchos*: subacute toxicity (5 days) LC_{50} > 5000 mg/kg feed

Effects on terrestrial plants

Acute toxicity	*Brassica napus, Glycine max, Avena sativa*: EC_{50} > 100 mg/kg soil d.wt

Bioconcentration

Bioconcentration factor (BCF)	*Lepomis macrochirus* edible: 61 (±09), whole fish: 72 (±14)
Depuration time	DT_{50} [days]: edible: 0.25 (±0.03), whole fish: 0.24 (±0.03)
Level of metabolites (%) in organisms accounting for > 10 % of residues	No metabolites identified

Chapter 6: Other End Points

Physical and chemical properties of DMSA

Vapour pressure	2.5 x 10^{-4} Pa at 20 °C; 4.9 x 10^{-4} Pa at 25 °C
Henry's Law Constant	3.8 x 10^{-5} Pa.m^3.mol^{-1}
Solubility in water	1.3 g/L at 20 °C
Dissociation constant	At 20 °C: 2.0 x 10^{-9}; pK(a) value: 8.7
Partition coefficient n-octanol/water	At 20 °C: P_{ow} = 39; log P_{ow} = 1.59

Appendix II: List of Intended Uses

Dichlofluanid has been evaluated for its intended use as an antifoulant (PT 21); data were provided and accepted in support of this intended use.

The products are intended for use by non-professional operators only.

Product Type	PT 21
Object and/or situation	Hulls of commercial and pleasure craft Immersed objects / structures
Product name	Alukote A Interspeed Ultra Variant
Packaging	20 L steel drum, 2.5 L and 0.75 L tinplate
Categories of User	Non-professionals
Organisms controlled	Algae, diatoms and other foulants
Formulation type	Solvent based
Concentration in formulation	Alukote A: 4.04 % dichlofluanid Interspeed Ultra Variant: 2.94 % dichlofluanid (+ 44.27 % copper oxide)
Application method/kind	Alukote A and Interspeed Ultra Variant: non-professional brushing and rolling
Applied amount per treatment	Coverage: 10.5 m^2/litre
Storage	In a well ventilated, dry place away from sources of heat and ignition

Data supporting dichlofluanid for its use against the intended target organisms have demonstrated sufficient efficacy for active substance approval to be recommended.

To date, there are no known resistance issues when using dichlofluanid against the target organisms.

Appendix III: List of studies

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
Published	Barrueco, C.; de la Pena, E.	1988	Mutagenic evaluation of the pesticides captan, folpet, captafol, Dichlofluanid and related compounds with the mutants TA102 and TA104 of Salmonella typhimurium. Mutagenesis. 1988 Nov; 3(6): 467-80. Not to GLP Published	No	_
Published	Heil, J., Reifferscheid, G.; Hellmich, D.; Hergenroder, M.; Zahn, R.K.	1991	Genotoxicity of the fungicide Dichlofluanid in seven assays. Environ Mol Mutagen. 1991; 17(1): 20-6. Not to GLP Published	No	_
IIA, 4.2.1.1.1		1979	Fish toxicity - Dichlofluanid - rainbow trout. Not to GLP Unpublished	Yes	Bayer CropScience AG
IIA, 4.2.1.1.1		1980	Fischtoxizitaet - Dichlofluanid - Goldorfe. Not to GLP Unpublished	Yes	Bayer CropScience AG
IIA, 4.2.1.1.1		1986a	Acute flow-through toxicity of Preventol A 4-S to Rainbow Trout (Salmo gairdneri). GLP Unpublished	Yes	Bayer Chemicals AG
IIA, 4.2.1.1.1		1986b	Acute flow-through toxicity of Preventol A 4-S to Bluegill Sunfish (Lepomis macrochirus). GLP Unpublished	Yes	Bayer Chemicals AG
A6.1.1		1978	Euparen 90 VM - Acute toxicity studies in rats, mice, guinea pigs, rabbits and cats. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.1.1		1962	Product KUE 13032c _ Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.1.1		1990	Dichlofluanid - Study for acute oral toxicity in rats. GLP Unpublished	Yes	Bayer CropScience AG
A6.1.1		1990	KUE 13032 C 90 VM - investigations of acute oral	Yes	Bayer CropScience

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
			toxicity in rats. Not to GLP Unpublished		AG
IIA, 4.2.1.2.1		1986	Acute flow-through toxicity of Preventol A 4-S to Daphnia magna. GLP Unpublished	Yes	Bayer Chemicals AG
IIA, 4.2.1.2.1		1983	Acute Toxicity of Dichlofluanid (90 % premix) to Water Fleas. Not to GLP Unpublished	Yes	Bayer CropScience AG
A3.3.2.1		2007	Henry“s law constant of N,N-dimethylsulfamide. Unpublished.	Yes	Bayer CropScience AG
IIA, 4.2.3.1		2004	Effects of Dichlofluanid on the phytotoxicity of non-target plants: seedling, emergence and seedling growth test. GLP Unpublished	Yes	Bayer Chemicals AG
A6.4.1		2004	Technical Grade Dichlofluanid (Euparen) - A 90-Day Subchronic Toxicity Feeding Study in the Beagle Dog. GLP Unpublished	Yes	LANXESS Deutschland GmbH
A6.4.1		1964	Report of 4-months feeding tests on rats with active ingredient Bayer 47531. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.6.1		1979a	KUE 13032 C - Salmonella/microsome test for the investigation of point-mutagenic effects. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.6.1		1979b	Preventol A 4 - Salmonella/microsome test for the investigation of point-mutagenic effects. Not to GLP Unpublished	Yes	LANXESS Deutschland GmbH
A6.6.1		1980a	Salmonella / Microsome test to investigate point-mutagenic action. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.6.1		1984	KUE 13032 C - Dichlofluanid - Salmonella/microsome test to evaluate for potential point mutation.	Yes	Bayer CropScience AG

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
			Not to GLP Unpublished		
A6.6.1		1978	Mutagenicity study of Euparen on bacterial systems. Not to GLP Unpublished	Yes	LANXESS Deutschland GmbH
A6.8.1		1989	A teratology study with Dichlofluanid (Euparen VM 90) in the rat. GLP Unpublished	Yes	Bayer CropScience AG
A6.8.1		1982	Embryotoxicity study in rabbits with oral application of KUE 13032 C (Dichlofluanid; a.i. of Euparen). GLP Unpublished	Yes	Bayer CropScience AG
A6.12.1		1989	Euparen and Euparen M - In-Company Occupational Medical Experience. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.12.1		1982	Statement to Pkt IV/1.2.2 of the BBA application form "Details of effects on man, internal company experience". Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.12.1		2004	Occupational Medical Experiences with Dichlofluanid. Not to GLP Unpublished	Yes	LANXESS Deutschland GmbH
IIA, 4.2.1.1.2		1989	Toxicity of Dichlofluanide techn. (VM 90) for Rainbow Trout (Salmo gairdneri) with prolonged exposure (21 days); including Amendment No.1 to report. GLP Unpublished	Yes	Bayer CropScience AG
IIA 4.2.1.1.2	Lowe, J.I.	1964	Effects of pesticides on marine animals. US Department of the Interior, Fish and Wildlife Service, USA Not to GLP. Published.	No	US Department of the Interior, Fish and Wildlife Service
IIA 4.2.1.1.2		2004a	Preventol A 4-S - Fish (Sheepshead Minnow), Acute Toxicity Test. Static, 96 h. GLP Unpublished	Yes	LANXESS Deutschland GmbH
A6.1.2		1986	Acute dermal toxicity of	Yes	LANXESS

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
			Preventol A 4-S in Albino Rabbits. GLP Unpublished		Deutschland GmbH
IIA, 4.2.1.2.2		2006b	Chronic Toxicity of Dichlofluanid technical to the Daphnia magna Under Flow-Through Conditions. GLP Unpublished	Yes	Lanxess Deutschland GmbH
IIA 4.2.1.2.2		2001 (amended 2006)	Thermal Stability of the agrochemical active ingredient dichlofluanid. Not to GLP Unpublished.	Yes	LANXESS Deutschland GmbH
IIA, 4.2.1.2.2		1989b	Influence of Dichlofluanid on the reproduction of Daphnia magna. GLP Unpublished	Yes	Bayer CropScience AG
IIA, 4.2.2.?		1986b	Subacute dietary LC50 of Preventol A4-S to Bobwhite Quail. GLP Unpublished	Yes	Bayer Chemicals AG
IIA, 4.2.2.?		1986c	Subacute dietary LC50 of Preventol A4-S to Mallard Ducks. GLP Unpublished	Yes	Bayer Chemicals AG
IIA 4.2.1.3.2		2004b	Preventol A 4-S - Amphipod (Corophium volutator), Acute Toxicity Test, Static, 10 d Limit Test in a Water-Sediment System. GLP Unpublished	Yes	LANXESS Deutschland GmbH
IIA, 4.2.3.2		1989	Toxicity of Euparen (WG) to Earthworms. Bayer AG HBF/RG 101 GLP Unpublished	Yes	Bayer CropScience AG
A3.3.2		2007	N,N-dimethylsulfamide, Vapour pressure A.4 (OECD 104). GLP. Unpublished.	Yes	Bayer CropScience AG
A6.3.2		2003	Dichlofluanid - Study for subacute dermal toxicity in rats. GLP Unpublished	Yes	LANXESS Deutschland GmbH
IIA	Callow, M.E.;	1995	A simple method to evaluate	No	N/A

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
4.2.1.4.2	Finlay, J.A.		the degradation of antifouling biocides. Biofouling, 1995, Vol. 9(2), pp 153-165. Not to GLP. Published.		
IIA 4.2.1.4.2		2004c	Preventol A 4-S Alga, Growth Inhibition Test with Skeletonema costatum, 96 h. GLP Unpublished	Yes	LANXESS Deutschland GmbH
A6.6.2		1985	Mutagenicity evaluation of KUE 13032 C (VM) - c.n. Dichlofluanid - in the mouse lymphoma forward mutations assay. GLP Unpublished	Yes	Bayer CropScience AG
A6.6.2		1986a	KUE 13032 C - Dichlofluanid - In vitro cytogenetic study on human lymphocyte cultures to evaluate for chromosome-damaging effects. GLP Unpublished	Yes	Bayer CropScience AG
A6.6.2		1989	Chromosome aberration assay in bone marrow cells of the Chinese hamster with KUE 13032 C. GLP Unpublished	Yes	Bayer CropScience AG
A6.8.2		1991	KUE 13032 C (c.n. Dichlofluanid) - Two-Generation Study on Rats. GLP Unpublished	Yes	Bayer CropScience AG
A6.8.2		1992	KUE 13032 C (c.n. Dichlofluanid) - Supplementary Two-Generation Study on Rats. GLP Unpublished	Yes	Bayer CropScience AG
IIA, 4.2.1.1.3		2006a	Early Life Stage Toxicity of Dichlofluanid technical to the Fathead Minnow (Pimephales promelas) Under Flow-Through Conditions. GLP Unpublished	Yes	Lanxess Deutschland GmbH
A6.1.3		1988	KUE 13032 C 90 VM 1146 B (Dichlofluanid) - Study for acute inhalation toxicity to the rat according to OECD Guideline GLP	Yes	Bayer CropScience AG

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
			Unpublished		
A6.1.3		2000	Preventol A 4-D (Dichlofluanid) – Study on acute inhalation toxicity in rats according to GLP Unpublished	Yes	LANXESS Deutschland GmbH
A6.1.3		1986	Acute inhalation toxicity study with Preventol A 4-S dust in rats. GLP Unpublished	Yes	LANXESS Deutschland GmbH
IIA, 4.2.3.3		1991a	Influence of the Commercial Product Euparen WG 50 on the Soil Respiration after Amendment with Glucose. GLP Unpublished	Yes	Bayer CropScience AG
IIA, 4.2.3.3		1991b	Influence of the Commercial Product Euparen WG 50 on the Microbial Mineralization of Carbon in Soils. GLP Unpublished	Yes	Bayer CropScience AG
IIA, 4.2.3.3		1991c	Influence of the commercial product Euparen WG 50 on Nitrogen Mineralization in Soil. GLP Unpublished	Yes	Bayer CropScience AG
A6.6.3		1988a	KUE 13032 C -Dichlofluanid - Mutagenicity study for the detection of induced forward mutations in the CHO-HGPRT assay in vitro. GLP Unpublished	Yes	Bayer CropScience AG
A6.6.3		1988b	KUE 13032 C - Dichlofluanid - Mutagenicity study for the detection of induced forward mutations in the V79-HGPRT assay in vitro. GLP Unpublished	Yes	Bayer CropScience AG
IIA, 4.2.1.4		1985	Growth Inhibition of Green Algae (Scenedesmus subspicatus) by Dichlofluanid (90 % Premix). Not to GLP Unpublished	Yes	Bayer CropScience AG
IIA, 4.2.1.4		1989a	Toxicity of Euparen M WG 50 to Scenedesmus subspicatus (OECD Algae Growth Inhibition Test). GLP Unpublished	Yes	Bayer CropScience AG

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
A6.1.4		1982	KUE 13032 C (Dichlofluanid) - Studies to determine a primary irritant effect on the skin and mucous membranes. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.1.4		1978	Preventol A 4 - Irritation of skin and mucosa. Not to GLP Unpublished	Yes	LANXESS Deutschland GmbH
IIA, 4.2.3.4		1986a	Acute Oral LD50 of Preventol A4-S to Bobwhite Quail. GLP Unpublished	Yes	Bayer Chemicals AG
IIA, 1.4.4		2005	Validation of analytical methods of Dichlofluanid and impurities in technical Dichlofluanid. GLP Unpublished	Yes	Lanxess Deutschland GmbH
IIA, 1.4.4		2003	Method for the determination of residues of Dichlofluanid and DMSA in soil-Validation of the DFG Method S19 (Extended and revised version). GLP Unpublished	Yes	Bayer Chemicals AG
IIA, 1.4.4		1992	Method for the determination of Dichlofluanid in air. Not to GLP Unpublished	Yes	Bayer CropScience AG
IIA, 1.4.4		2003	Validation of an analytical method (analogous to DFG Method W5) for the determination of residues of N-N-Dimethyl-N`-Phenylsulphamide (DMSA) in drinking and surface water. GLP Unpublished	Yes	Bayer Chemicals AG
IIA, 1.4.4		1999	Validation of an analytical method (analogous to DFG method W 5) for the determination of residues of Dichlofluanid in drinking and surface water. GLP Unpublished	Yes	Bayer Chemicals AG
A6.6.4		1988	Ex Vivo hepatocyte UDS study with KUE 13032 C. GLP Unpublished	Yes	Bayer CropScience AG
A6.6.4		1978	KUE 13032 C - Micronucleus test for mutagenic effects on	Yes	Bayer

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
			mice. Not to GLP Unpublished		CropScience AG
A6.6.4		1988a	KUE 13032 C - c.n. Dichlofluanid - In vivo study of the bone marrow in Chinese hamsters to evaluate for a chromosome-damaging effect. GLP Unpublished	Yes	Bayer CropScience AG
A6.1.5		1980a	Preventol A 4 - Study on Guinea Pigs for sensitizing effect ("Draize test"). Not to GLP Unpublished	Yes	LANXESS Deutschland GmbH
A6.1.5		1980b	Preventol A 4 - Study for sensitizing effect in the open epicutaneous test. Not to GLP Unpublished	Yes	LANXESS Deutschland GmbH
A6.1.5		1980	Preventol A 4 - Study for sensitising effect (Magnusson and Kligman's maximisation test). Not to GLP Unpublished	Yes	LANXESS Deutschland GmbH
A3.3.5		2007a	Water solubility of N,N-dimethylsulfamide at pH 5, pH 7 and pH 9 (Flask method). GLP Unpublished	Yes	Bayer CropScience AG
A6.6.5		1988b	KUE 13032 C - Dichlofluanid - Spot Test on cross-bred C57B1/6J x T stock mouse fetuses to evaluate for induced somatic changes in the genes of the coat pigment cells. GLP Unpublished	Yes	Bayer CropScience AG
A.6.6.5		1974a	KUE 13032 C (active ingredient of Euparen) - dominant lethal study to investigate mutagenic potential. Not to GLP Unpublished	Yes	Bayer CropScience AG
IIA, 4.2.1.6		2001	Preventol A 4-S - Toxicity to Bacteria. Bayer AG GLP Unpublished	Yes	Bayer Chemicals AG
A6.6.6		1986b	KUE 13032 C - Dichlofluanid - Dominant lethal test on the male mouse to assess for mutagenic effects. GLP	Yes	Bayer CropScience AG

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
			Unpublished		
IIA, 4.2.1.7		1991	Dichlofluanid - Bioconcentration in Fish. GLP Unpublished	Yes	Bayer CropScience AG
IIA, 1.3	Bayer Chemicals	2003	Safety Data Sheet "Preventol A 4-S" Bayer AG 014730/ 28 Not to GLP Published	No	_
IIA, 1.3		2003	Determination of safety-relevant data of Preventol A 4-S. GLP Unpublished	Yes	Bayer Chemicals AG
IIA, 1.3		2001	Physicochemical Properties of Dichlofluanid. GLP Unpublished	Yes	Bayer Chemicals AG
IIA, 1.3		2004	Solubility of Dichlofluanid techn. (Euparen tech) in organic solvents. GLP Unpublished	Yes	Bayer AG
IIA, 1.3		1986	Thermal Stability of the agrochemical active ingredient dichlofluanid. Bayer AG 86/1046TA Not to GLP Unpublished	Yes	Bayer CropScience AG
IIA, 1.3		1999	Density and vapour pressure of Dichlofluanid-DMSA Not to GLP Unpublished	Yes	Bayer CropScience AG
IIA, 1.3		1986	Dichlofluanid - Spectra of the active ingredient. Not to GLP Unpublished	Yes	Bayer CropScience AG
IIA, 1.3		1985	Water Solubility of DMSA. Not to GLP Unpublished	Yes	Bayer CropScience AG
IIA, 1.3		1989	Octanol/water partition coefficient of Dimethylsulfanilide (DMSA) Not to GLP Unpublished	Yes	Bayer CropScience AG
IIA, 1.3		2001	Surface Tension, Physical-chemical Properties of Dichlofluanid. GLP Unpublished	Yes	Bayer Chemicals AG

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
IIA, 1.3		1989	Dissociation constant of DMSA Not to GLP Unpublished	Yes	Bayer AG
IIA, 1.3		2001	Melting point of KUE 13032C (Dichlofluanid). GLP Unpublished	Yes	Bayer Chemicals AG
IIA, 1.3		2002	Partition coefficient in Octanol-Water, Water Solubility and pKa value in dependence on temperature of KUE 13032 C (Dichlofluanid). GLP Unpublished	Yes	Bayer Chemicals AG
IIA, 1.3		1994	Vapour Pressure - Dichlofluanid (Euparen). GLP Unpublished	Yes	Bayer CropScience AG
IIA, 1.3		2004	Dichlofluanid technical, Preventol A 4-S, Preventol A 4-D, Preventol A 4-F, Corrosion Characteristics, Packaging Materials. Not to GLP Unpublished	Yes	Bayer Chemicals AG
A4 4.2		2004b	Determination of residues of dichlofluanid and its metabolite DMSA in water and marine sediments of Greek marinas in the spring and in the summer of 2003. GLP Unpublished	Yes	LANXESS Deutschland GmbH
A4 4.2		2004c	Determination of residues of dichlofluanid and its metabolite DMSA in water and marine sediments at suspected hotspots of Greek marinas in the spring and in the summer of 2003. GLP Unpublished	Yes	LANXESS Deutschland GmbH
A4 4.2		2004d (amend. 2004)	Determination of residues of dichlofluanide and its metabolite DMSA in water and marine sediments of Greek marinas in the summer of 2003. GLP Unpublished	Yes	LANXESS Deutschland GmbH
A4 4.2		2004e	Determination of residues of dichlofluanide and its metabolite DMSA in water and marine sediments at suspected	Yes	LANXESS Deutschland GmbH

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
			hotspots of Greek marinas in the summer of 2003. GLP Unpublished		
A4 4.2		2004	Validation of analytical methods for the determination of dichlofluanide and its metabolite DMSA (dimethylaminosulphanilide in seawater and marine sediment. GLP. Unpublished.	Yes	LANXESS Deutschland GmbH
A4, 4.2		2007	Method 01041 for the determination of N,N-dimethylsulfamide in water by HPLC-MS/MS. Non GLP Unpublished	Yes	Bayer CropScience AG
A6.2		1986	Structural clarification of metabolites of [ring-U-14C]dichlofluanid in rat feces. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.2		1968	Studies on the metabolism of BAY 47531. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.2		1978	Biotransformation of [14C] Dichlofluanid in the Rat. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.2		1985	(Phenyl-U-14C)Dichlofluanid - Biokinetics Part of general metabolism study on rats. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.2		1977	(14C)Dichlofluanid (active ingredient of Euparen) – Biokinetic study on rats. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.4		1966	Bayer 47531 - Subchronic toxicological study on dogs. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.5		2004	Technical grade Dichlofluanid (Euparen VM 90): Oral dosing chronic toxicity studies in the beagle dog; Determination of NOEL/NOAEL. LETTER Not to GLP Unpublished	Yes	LANXESS Deutschland GmbH

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
A6.5		1992	Technical grade Dichlofluanid (Euparen VM 90): Oral dosing chronic toxicity studies on the Beagle dog. GLP Unpublished	Yes	Bayer CropScience AG
A6.5		1996	Addendum to the original Bayer report: Technical grade Dichlofluanid (Euparen VM 90): Oral dosing chronic toxicity studies on the Beagle dog. GLP Unpublished	Yes	Bayer CropScience AG
A6.5		1997	Supplemental submission: Technical grade Dichlofluanid (Euparen VM 90): Oral dosing chronic toxicity studies on the Beagle dog. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.5		1982	KUE 13032 C (Dichlofluanid, Euparen(R) active ingredient) - Chronic toxicological study on mice (feeding experiment over 2 years). Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.5		1968	BAY 47531 - Chronic toxicological studies on rats. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.5		1969a	Chronic toxicity studies on dogs (two-year feeding experiment). Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.5		1969b	BAY 47531 - Generation study on rats. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.5		1969	Pathology Report of the chronic toxicity of compound BAY 47531 in rats. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.5		1969	Pathology Report of BAY 47531 Two Year Dog Study Not to GLP Unpublished	Yes	Bayer CropScience AG

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
A6.6		1979c	KUE 13032 C - Cytogenetic studies of spermatogoniae of Chinese hamsters to test for mutagenic effects. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.6		1980b	KUE 13032 C - Sister chromatid exchange on the Chinese hamster in vivo to evaluate for mutagenic effect. Not to GLP Unpublished	Yes	Bayer CropScience AG
A 6.5/6.7		1993a	KUE 13032 C (Dichlofluanid) - Study on chronic toxicity and carcinogenicity in Wistar rats (administration in food over 105 weeks). GLP Unpublished	Yes	Bayer CropScience AG
A6.7		1993b	KUE 13032 C (Dichlofluanid) - Study for oncogenicity in B6C3F1 mice (administration in feed over 2 years). GLP Unpublished	Yes	Bayer CropScience AG
A 6.5/6.7		1994a	KUE 13032 C (Dichlofluanid) - Study on chronic toxicity and carcinogenicity in Wistar rats (administration in food over 105 weeks). GLP Unpublished	Yes	Bayer CropScience AG
A6.7		1994b	KUE 13032 C (Dichlofluanid) - Study for oncogenicity in B6C3F1 mice (administration in feed over 2 years). GLP Unpublished	Yes	Bayer CropScience AG
A6.8		1974b	KUE 13032 C: studies for embryotoxic and teratogenic effects on rats following oral administration. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.10		1981	KUE 13032c: Subchronic toxicological study to ascertain the dose-time relationship in the effect on the thyroid (feeding study over 9 weeks). Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.10		1981	Effect of subchronic KUE 13032C (Euparen active ingredient) administration on	Yes	Bayer CropScience

Reference	Author	Date	Study title	Data Protection claimed	Data Owner
			the thyroid function in male rats. Not to GLP Unpublished		AG
A6.12		2003a	Occupational Medical Experiences with Dichlofluanid in the FU-Plant, Dormagen. Not to GLP Unpublished	Yes	Bayer CropScience AG
A6.12		2003b	Occupational Medical Experiences with Dichlofluanid in the FL-Plant, Dormagen. Not to GLP Unpublished	Yes	Bayer CropScience AG