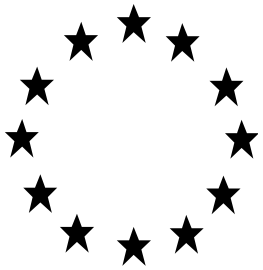
Regulation (EU) n°528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



4,5-Dichloro-2-octyl-2H-isothiazol-3-one (DCOIT)

Product type 21 (Antifouling products)

March 2014

Norway

Finalised in the Standing Committee on Biocidal Products at its meeting on 13 March 2014

TABLE OF CONTENTS

1 STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1 PRINCIPLE OF EVALUATION

This Assessment Report has been established as a result of the evaluation of 4,5-Dichloro-2-octyl-2H-isothiazol-3-one (DCOIT) in product type 21 (antifouling products), carried out in the context of the work program for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with the original view to the possible inclusion of this substance into Annex I or IA to that Directive.

The evaluation has therefore been conducted in the view to determine whether it may be expected, in light of the common principles laid down in Annex VI to Directive 98/8/EC, that there are products in product type 21 containing DCOIT that will fulfill the requirements laid down in Article 5(1) b), c) and d) of that Directive.

1.2 PURPOSE OF THE ASSESSMENT

The aim of the Assessment Report is to support a decision on the approval of DCOIT for product type 21, and should it be approved, to facilitate the authorisation of individual biocidal products in product type 21 that contain DCOIT. 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.

The conclusions of this report were reached within the framework of the uses that were proposed and supported by the Applicant (see Appendix II). An extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Regulation (EU) No 528/2012.

For the implementation of the common principles of Annex VI, the content and conclusions of this Assessment Report 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 has been granted.

[1] Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1

1.3 PROCEDURE FOLLOWED

This Assessment Report has been established as a result of the evaluation of DCOIT in product type 21 (antifouling products), carried out in the context of the work program for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market.

DCOIT (CAS no. 64359-81-5) was notified as an existing active substance by Rohm and Haas Europe Trading ApS; a subsidiary of The Dow Chemical Company, hereafter referred to as the Applicant, in product type 21.

Commission Regulation (EC) No 1451/2007 of 4 December 2007[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 7(1) of that Regulation, Norway was designated as Rapporteur to carry out the assessment on the basis of the dossier submitted by the Applicant. The deadline for submission of a complete dossier for DCOIT as an active substance in Product Type 21 was 30 April 2006, in accordance with Article 9 (c) of Regulation (EC) No 1451/2007.

On 28 February 2006, the Rapporteur received a dossier from the Applicant. The Rapporteur accepted the dossier as complete for the purpose of the evaluation on 16 June 2006.

On 21 December 2010, the Rapporteur submitted, in accordance with the provisions of Article 14(4) and (6) of Regulation (EC) No 1451/2007, to the Commission and the Applicant a copy of the evaluation report, hereafter referred to as the Competent Authority Report. The Commission made the report available to all Member States by electronic means on 3 February 2011. The Competent Authority Report included a recommendation for the inclusion of DCOIT in Annex I to the Directive for product type PT21.

In accordance with Article 16 of Regulation (EC) No 1451/2007, the Commission made the Competent Authority Report publicly available by electronic means on 8 February 2011. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

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 organized by the Commission. Revisions agreed upon were presented at Technical and Competent Authority Meetings, and the Competent Authority Report was amended accordingly.

In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present Assessment Report contains the conclusions of the Standing Committee on Biocidal Products, as finalized during its meeting held on 13 March 2014.

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

2 OVERALL SUMMARY AND CONCLUSIONS

2.1 IDENTITY, INTENDED USES, EFFICACY AND CLASSIFICATION OF THE ACTIVE SUBSTANCE

2.1.1 Identity and analysis

The identity and the physical/chemical properties of 4,5-Dichloro-2-octyl-2H-isothiazol-3-one (DCOIT) have been summarized in the Document II-A and in the confidential part of the dossier. Physical/chemical properties are also listed in the List of Endpoints.

GLP-validated methods for analysis of DCOIT and impurities in the active substance as manufactured and in the biocidal products have been provided. 5-batch analysis from the different production sites were submitted with the original dossier for the evaluation of DCOIT in the different product types. These data have been considered sufficient for the evaluation of the relevance of the toxicological and ecotoxicological studies submitted. However, as the purity of the raw material has been reported to have increased and the analyses are up to 10 years old, new 5-batch analyses from present production sites should be submitted at the latest 6 months prior to the date of approval to the original Rapporteur Member State (Norway) and evaluated by the RMS. This would also be of value for establishing a reference source for future possible technical equivalence evaluation of other sources for DCOIT.

GLP-validated methods for analysis of DCOIT in environmental matrices (soil and sediments, air, drinking-, sea- and surface water, fish and shellfish) have been provided. The limits of quantification were 0.05 µg/g in soil and sediments, 0.2 µg/m^3 in air, 0.02 µg/L in water and 0.01 mg/kg in fish and shellfish tissues. According to the addendum "Additional guidance on: TNsG on Data Requirements, Part A, Chapter 2, Point 4 Analytical Methods for Detection and Identification", confirmatory methods are needed for the soil and fish and shellfish method, respectively, because in the principal methods only two (soil) respective one (fish/shellfish) ions were validated. The missing data on the third fragment ion for the soil method are to be provided at the latest 6 months prior to date of approval to the original Rapporteur Member State (Norway). Alternatively, a suitable justification should be provided if the additional ions cannot be identified due to the small size of the molecule. The missing data on the second fragment ion for the fish and shellfish HPLS/MS/MS study is to be provided at the latest 6 months prior to date of approval to the original Rapporteur Member State (Norway). If a second ion cannot be identified due to the small size of the molecule, confirmation can be addressed by a different approach. However, new information submitted recently, which is not fully evaluated yet, indicate that the residues in fish consist of metabolites which are rapidly excreted and not parent material. If this fact is confirmed, the data requirement for further analytical validation is redundant.

No analytical data for the major metabolites of the water and water-sediment simulation studies are available. No final conclusion can be drawn whether analytical methods for these four major metabolites are necessary at the moment as there is still an ongoing discussion on

the classification of DCOIT as N R50/53 / Aquatic chronic 1 based on the properties of its metabolites. As long as this issue is not finally concluded no decision can be drawn.

2.1.2 Intended uses

DCOIT is used as a broad spectrum biocide in antifouling paints (product type 21) to control the growth and settlement of fouling organisms on commercial boats and superyachts (size > 25 m), and on buoys, sluice doors and off-shore structures submerged in marine and brackish/estuarine water. DCOIT is used at 1-3 % in the antifouling paint (typical concentration 2%), as a co-biocide with another biocidal active substance such as copper oxide. The antifouling paints are ready for use products which are applied by trained professionals. The application is done by high pressure airless spraying and for spot applications (or small objects) by brush and roller. One to up to 3 coats of antifouling paint may be applied depending on the conditions of use and the service life recommended. DCOIT-containing antifouling paints are intended for professional use only. The general public will therefore not be exposed to the active substance in the normal conditions of use.

Two products were included as representative formulations in this CA-report for Annex I inclusion:

- A theoretical product of the Applicant containing 3% DCOIT
- A real product (Antifouling Globic 81900), which is a self- polishing TBT-free antifouling coating, containing 2 % DCOIT and cuprous oxide

The composition of these products can be found in the confidential section of the CA-report.

For the purpose of the present risk assessment for the DCOIT, the second active ingredient, as well as potential substances of concern, were not addressed.

2.1.3 Efficacy

DCOIT is a broad spectrum antifouling agent for preventing the growth and settlement of soft fouling (bacteria, fungi, algae) and hard fouling (barnacles) organisms on submerged surfaces. DCOIT exhibits rapid inhibition of growth at very low levels and cidal effects at higher levels or for longer contact periods.

DCOIT was shown to be a highly effective antimicrobial agent when tested in standard biocide efficacy tests. Minimum Inhibitory Concentration (MIC) studies were conducted to demonstrate the lowest level of biocide which inhibits the growth of soft fouling (or slime-forming) microorganisms (bacteria, algae, fungi). The results showed that DCOIT was effective at concentrations ranging from <0.01 to 8.0 parts per million (ppm) for the 85 strains of microorganisms tested. Additional studies with the green marine algae, *Enteromorpha*, and the marine diatom, *Amphora,* showed DCOIT as highly effective with LD50 values of 2.0 and 3.4 parts per billion (ppb), respectively. Lethality studies with marine barnacles showed DCOIT as highly effective at 0.34 ppm (LD50) for control of *Balanus nauplius* larvae.

Field tests conducted on some DCOIT containing real products, which also contain copper oxide as active substance, confirmed that the addition of DCOIT to copper-containing paints increase their efficacy and ensure a very good control of the fouling organisms. In these trials,

an enhanced antifouling effect is indicated when adding 0.4, 0.8 or 1.3 % DCOIT to the cuprous oxide containing antifouling formulation, respectively.

The mode of action of DCOIT has been studied and it has been shown that DCOIT reacts with the proteins of organisms that come in contact with the coating surface (for example, algae, seaweed, barnacles). This results in interruption of the metabolic processes that utilize these proteins. Fouling organisms initiate specific physiological activities involved in attaching to solid surfaces that are disrupted by DCOIT. As a result the organisms do not successfully colonize the treated surfaces and biofouling is minimized.

DCOIT has been used as a commercial antifouling agent since 1986, and no problems of resistance have been observed. There are also no published reports of microbial resistance to DCOIT. This is likely due to its unique mechanism of action, broad spectrum of activity, use concentrations, and pattern of use.

2.1.4 Classification

The proposed classification and labeling of 4,5-Dichloro-2-octyl-2H-isothiazol-3-one (DCOIT) according to the principles given in Annex VI of Council Directive 67/548/EEC (with amendments and adaptations) is presented in Table 2.1.

Table 2.1: Proposed classification according to Directive 67/548/EEC*

Proposed classification	T+; R26, Xn; R21/22, C; R34, Xi; R43 - R37, N; R50/53**
Proposed labelling	
Symbol letter:	T+, C, N
Indication of danger	Very toxic Corrosive Dangerous for the environment
Labelling symbol	
R phrases	R21/22: Harmful in contact with skin and if swallowed R26: Very toxic by inhalation R34: Causes burns R37: Irritating to respiratory system R43: May cause sensitization by skin contact R50/53**: Very toxic to aquatic organisms; may cause long-term adverse effects in aquatic environments
S phrases	S22: Do not breathe dust. S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S28: After contact with skin, wash immediately with plenty of … (to be specified by the manufacturer) S36/37/39: Wear suitable protective clothing, gloves and eye/face protection. S45: In case of accident or if you feel unwell, seek medical advice immediately (show label where possible). S57: Use appropriate containment to avoid environmental contamination. S60: This material and its container must be disposed of as hazardous waste.
Specific concentration limits	Setting specific lower concentration limits for sensitisation is warranted A specific concentration limit of 0.001% is proposed ***. Setting specific concentration limits for corrosion/irritation should be considered. DCOIT's high aquatic toxicity warrants specific concentration limits for the environmental effects. A M factor of 100 will be applied, due to the 24 hours E_rC_{50} of 1.6 µg/L from the *N. pelliculosa* study.

*No final decision made at the time of publication of this report. The final classification will be established by ECHA.

**See discussion below Table 2.2

*** Proposal based on animal data. A higher concentration limit has been proposed by the Applicant based on human data. To be further discussed by the Risk Assessment Committee under ECHA.

Table 2.2 presents the proposed classification and labelling of 4,5-Dichloro-2-octyl-2H-isothiazol-3-one (DCOIT) according to the new CLP regulation ((EC) No 1272/2008), incorporating GHS into EUs regulation).

Table 2.2: Proposed classification according to the CLP regulation*

Proposed classification	Acute Tox 4 (oral) Acute Tox 4 (dermal) Acute Tox 1 (inhalation) Skin Corr 1C STOT SE 3 Skin Sens. 1A ** Aquatic chronic 1***
Proposed hazard statement	H302: Harmful if swallowed H312: Harmful in contact with skin H330: Fatal if inhaled H314: Causes severe skin burns and eye damage H335: May cause respiratory irritation H317: May cause an allergic skin reaction H410: Very toxic to aquatic organisms with long lasting effects***
Specific concentration limits	Setting specific lower concentration limits for sensitisation is warranted. A specific concentration limit of 0.001% is proposed.**** Setting specific concentration limits for corrosion/irritation should be considered. DCOIT's high aquatic toxicity warrants specific concentration limits for the environmental effects. An M factor of 100 will be applied, due to the 24 hours E_rC_{50} of 1.6 µg/L from the *N. pelliculosa* study.

* No final decision made at the time of publication of this report. The final classification will be established by ECHA.
** Classification according to criteria in 2. ATP to the CLP Regulation
*** See discussion below.
**** Proposal based on animal data. A higher concentration limit has been proposed by the Applicant based on human data. To be further discussed by the Risk Assessment Committee under ECHA.

***** Discussion on environmental classification: N R53 (Aquatic chronic 1)**

Simulation tests show rapid primary biodegradation of DCOIT in the environment to metabolites which are 2-5 orders of magnitude less toxic than DCOIT. However, ultimate biodegradation of DCOIT could not be demonstrated. Due to uncertainties regarding environmental fate and behaviour and ecotoxicity of the major metabolites formed in the aquatic simulation tests, no definite conclusion can be drawn at the moment whether N R50 (Aquatic acute 1) or N R50/53 (Aquatic chronic 1) would be the most appropriate classification for DCOIT. It is therefore suggested forwarding this issue to a classification and labelling expert group.

2.2 SUMMARY OF THE RISK ASSESSMENT

2.2.1 Human health risk assessment

2.2.1.1 Hazard identification and effect assessment of active substance

Toxicity studies with DCOIT and preformulations of DCOIT (approximately 30% DCOIT in xylene) have been conducted in laboratory animals to identify the potential adverse effects of DCOIT in humans.

Absorption, distribution, metabolism and excretion

A toxicokinetic study indicated that following oral administration of ^{14}C-labelled DCOIT to rats at dosages of 20 and 250 mg/kg, practically all of the ^{14}C-label was rapidly excreted within a 2 day period, primarily in the faeces, and by 4 days, only negligible amounts remained in the tissues and residual carcass. Plasma half-life's between 16-25 hrs were determined. Close to 20% of DCOIT was excreted in the urine following oral administration. As the contribution of biliary excretion to the elimination of DCOIT is not known, the amount of DCOIT in the faeces that has actually been absorbed is uncertain. As the main metabolites in the faeces may have been formed by biodegradation in the GI tract, they do not give additional information about the oral absorption of DCOIT. In conclusion, the oral absorption is assumed to be moderate, and the value 20% is taken forward to the risk characterization.

DCOIT is extensively metabolised following oral administration. Metabolism of DCOIT primarily involves cleavage of the ring and subsequent oxidation. The major metabolite identified was N-(n-octyl) malonamic acid (NNOMA). Results also suggested that DCOIT will not bioaccumulate significantly.

Absorption via the respiratory system has not been studied. However, an inhalation absorption value of 100% is taken forward to the risk characterization as a worst case value.

A high penetration of DCOIT dissolved in acetone (0.045% and 3% DCOIT) or dipropylene glycol monoethyl ether, DPGME (0.25 % DCOIT) into the skin of rats has been shown. Dermal delivery factors between 17% and 70% are estimated, dependent of exposure duration and observation times. The dermal delivery of DCOIT in DPGME through human skin was found to be 17%. However, there are conflicting results of studies with human skin which makes it uncertain whether it is correct to assume a lower human than rat dermal delivery value.

During a 30 day period, following a 24h exposure of rats to DCOIT in DPGME, 49% was absorbed. This study shows that most of the DCOIT that penetrates the skin will over time be systemically available, probably in a metabolised form. However, the absorption rate is relatively low and 24% or less of the administered dose was systemically available in a 3 day period following DCOIT administration. Hair follicles seem to be major portals of entry for DCOIT.

The Rapporteur suggests a dermal delivery value of 51% for DCOIT in concentrations of 0.25%-1.9% and 31% for DCOIT concentrations of 2% or above based on rat studies and systemic available doses of 24% for DCOIT in concentrations of 0.25%-1.9% and 22% for DCOIT concentrations above 2%.

However, DCOIT is corrosive in higher concentrations. The dermal absorptions values are not relevant for damaged skin.

A summary of the dermal absorption values can be found in the table below.

Table 2.3. Dermal absorption values for DCOIT and formulations thereof

Concentration.	0.25-1.9%DCOIT	≥2% DCOIT
Dermal absorption	51% (dermal delivery) 24% (systemic available dose)	31% (dermal delivery) 22% (systemic available dose)

The results obtained from two studies of absorption of DCOIT from antifouling paint formulations suggest that the absorption of DCOIT in an antifouling paint formulation through human epidermis is low when compared with the absorption of DCOIT diluted in solvent without polymer. Based on these studies a dermal absorption value of 6% was derived (see chapter 2.2.1.2). This value was used in the risk assessment for both Antifouling Globic 81900 and the theoretical product. However, as the dermal penetration of DCOIT is highly formulation-dependent, studies on the actual formulations or argumentation for read across from related formulations should be provided in the product authorisation.

In lack of such data, the referred values in the table should be used as reasonable worst case values in the risk characterization for DCOIT and formulations containing DCOIT

Acute toxicity

DCOIT is moderately toxic by ingestion of a single oral dose (oral LD_{50} was 1636 and 567 mg/kg bw in rats and mice, respectively). No acute dermal toxicity study with DCOIT technical is reported. However,in an acute dermal study on an antifoulant preformulation (C-9211 HQ, commercial product called SEA-NINE™ 211 Antifouling agent; 32.6% DCOIT in xylene) no mortality was observed at the highest dose tested (2000 mg/kg bw, equivalent to 652 mg DCOIT/kg bw). However, clear toxic effects were noted. In an acute inhalation toxicity test where rats were exposed for DCOIT aerosols, a LC_{50} value of 0.26 mg/L was determined.

According to Annex VI of Directive 67/548/EEC, DCOIT should be classified as Harmful if swallowed (Xn; R22). The LC_{50} value of 0.26 mg/L/4h (nose only exposure, mixture of aerosol and vapour of DCOIT Technical) is on the borderline between classification of DCOIT as toxic (T; R23) or very toxic (T+; R26) by inhalation. The cut off for classification with R26 is 0.25 mg/l/4h for aerosols and 0.5 mg/l/4h for vapours. The exact ratio of vapour to aerosol during the test is not known. However a significant portion of the exposure atmosphere seemed to contain vaporised test material. A classification with T+; R26 is proposed.

The information provided is insufficient for a classification for acute dermal toxicity. However, classification of DCOIT also for acute dermal toxicity (Xn; R21) could be considered.

Irritation/corrosivity

DCOIT and concentrated biocides are considered to be corrosive to skin and eyes.

DCOIT has not been tested in an *in vivo* irritation test. However, the antifoulant preformulation, C-9211 HQ (32.6% DCOIT in xylene) was found to be corrosive in a rabbit skin irritation test. Furthermore, a product containing 20% DCOIT in phenoxypropanol was found to be corrosive in a single-animal test performed in accordance with the OECD guideline 404. DCOIT was found to be non-corrosive in an *in vitro* skin corrosion test. However, the result of the *in vitro* test is suspected to be a false negative. Based on the corrosive nature of the antifoulant preformulation and DCOIT in phenoxypropanol, and on results on primary irritation in skin sensitisation studies in animals (a 0.01% concentration equivalent to a dose of 4.4 µg DCOIT/cm^2 was the highest non-irritating concentration/dose observed in the Guinea pig maximisation test, GPMT), DCOIT is regarded as corrosive to skin and eyes. This conclusion is supported by the corrosive properties of structurally related isothiazolinones. Classification as corrosive to skin (C; R34) is proposed.

An acute inhalation toxicity study (DCOIT Technical) and a 13 week repeated dose inhalation study in rats (preformulation of DCOIT in xylene) both indicate that DCOIT is a potent respiratory irritant. These results were supported by an upper airway sensory irritation test in rats (preformulation of DCOIT in xylene). Based on these results, a classification as irritant to respiratory tract (Xi; R37) is proposed.

Setting specific concentration limits should be considered.

Sensitization

DCOIT solved in ethanol is a local skin sensitizer at ≥ 0.01% (≥ 100 ppm; ≥ 4.4 µg a.i./cm^2) in a Guinea pig maximisation test (GPMT).

The major metabolite of DCOIT, N-(n-octyl) malonamic acid (NNOMA) is not considered a sensitizer at concentrations of 3%, 10% or 30% in a local lymph node assay.

The GPMT assay and supporting studies warrants the classification of DCOIT as a skin sensitizer (Xi; R43).

Setting lower specific concentration limits should be considered. In accordance with Guidance to Regulation (EC) No 1272/2008 on classification, labeling and packaging (CLP) of substances and mixtures (ECHA, 2009), DCOIT should be categorised as an extreme sensitizer based on the GPMT assay with a specific concentration of 0.001%[3].

No studies addressing respiratory sensitisation of DCOIT has been reported, and it is thus not possibly to evaluate the potential for respiratory sensitisation. Due to its high skin sensitising potential and considering its mode of action (binding to nucleophilic sites in proteins) DCOIT may be sensitising also via inhalation. However, the Applicant states that after 30 years of use, the Applicant is not aware of any information from workers or downstream users indicating that DCOIT may be a respiratory sensitizer. No classification is proposed for respiratory sensitisation.

[3] A higher concentration limit has been proposed by the Applicant based on human data. To be further discussed by the Risk Assessment Committee under ECHA.

Repeated dose toxicity

DCOIT was administered orally by gavage for 1 month (28 days) in the rat and by diet for 3 months (90 days) in the rat and dog. For the most part toxicity was observed at the site of dosing (i.e., histopathology of stomach and lower intestinal track). Minimal systemic toxicity was observed.

The lowest NO(A)EL in these tests was 10 mg/kg bw/day in dogs (3 months study). Reduced body weights and food consumption as well as changes in some hematological and clinical parameters were observed at the next dose level (45.9 (females)/47.5 (males) mg/kg bw/day).

From the oral gavage study in rats (1 months study) a NOAEL of 20 mg/kg bw/day and a LOAEL of 100 mg/kg bw/day was derived. Changes in clinical chemistry and haematology parameters were observed at 100 and 500 mg/kg bw. The changes indicate liver toxicity, but histology revealed no liver changes. DCOIT administration produced a dose-dependent increase in irritation of the gastrointestinal tract as well as effects on spleen and adrenal cortex.

The 90 days dog study and the 28 days rat study were selected for the risk assessment of systemic effects.

In a 21 day dermal study in rabbits 1 and 5 mg/kg bw/day of a preformulation C-9211M (35% DCOIT in mixed xylenes) was administered. Under these test conditions, skin irritation was the only toxic response reported. Slight skin irritation was seen in the low dose group, and moderate to severe skin irritation was seen in the high dose group. A systemic NOAEL of 1.75 mg DCOIT /kg bw/day (5 mg/kg bw/day of the preformulation) was derived, the highest dose administered. A LOAEL for local irritation of 0.35 mg DCOIT/kg bw/day, i.e. 0.035% (1 mg/kg bw/day of the preformulation) was derived.

In an inhalation study, rats received nose-only exposure of DCOIT (aerosol, 32.6% DCOIT in o-xylene) for 6 hours per day, 5 days per week for 13 weeks at concentrations up to 6.72 mg a.i/m^3. From this study a NOAEC of 0.02 mg DCOIT/m^3 was derived based on the histopathological changes seen in the nose and larynx at higher exposures. The LOAEC was 0.63 mg DCOIT/m^3.

The 13 week inhalation study in rats was selected for the risk assessment of local respiratory effects.

For the most part, toxicity was observed at the site of dosing in the repeated toxicity studies. Minimal systemic toxicity was observed at doses below those giving rise to local irritation.

Reproductive toxicity

In a 2-generation reproduction study in the rat, DCOIT was shown not to be a reproductive hazard. The NOAEL for parental toxicity was 400 ppm diet (30-41 mg/kg bw/day) based on clinical signs and body weight changes at higher doses. No changes were observed in reproductive performance (mating or fertility); gestation, lactation or viability indices; offspring viability; estrus cycle or sperm parameters; or pathology of reproductive organs at concentrations up to and including 800 ppm (62-93 mg/kg bw/day). Offspring viability was decreased at 3200 ppm (235-259 mg/kg bw/day). The NOAEL for systemic toxicity to

offspring was 200 ppm (16-21 mg/kg bw/day) based on reduced pup body weight at PND21 at 400 ppm and reduced thymic weight at 400 ppm in the F2 generation. The significance of the latter finding was supported by changes in thymic histopathology at 800 ppm (62-93 mg/kg bw/day). The effects on the thymus are possibly secondary to the reduced weight gain that was observed at the time of weaning when the pups start to depend on the intake of DCOIT treated foods.

Exposure to DCOIT induced indications of delayed puberty in offspring (delayed vaginal opening and preputial separation). However, these findings were not accompanied by changes in ano-genital distance, and no treatment-related alterations of male or female mating or fertility parameters were reported. Thus DCOIT is not considered toxic to reproduction.

Developmental toxicity testing in rats and rabbits indicated that DCOIT is toxic to dams and fetuses, but not teratogenic. Three developmental toxicity studies have been performed. In the most recent study, pregnant rats were exposed to doses of 10, 30 and 100 mg/kg bw/day of DCOIT technical and the NO(A)ELs for maternal and fetal toxicity in rats were determined to be 10 and 30 mg/kg bw/day, respectively. This is the only study with DCOIT technical and is considered the key developmental study. Maternal signs of toxicity included scant/soft faeces, diarrhea, reduced feed consumption and reduced weight gain. There was an increased number of litters which had fetuses with wavy ribs in the 100 mg/kg/day dose group.

In the two remaining studies, pregnant rabbits and rats were exposed to a preformulation (C-9211 and C-9211M) containing 40 and 49% active ingredient in xylene. In the rat study a NOAEL value of 11.2 mg DCOIT/kg bw/day is suggested for both maternal and fetal toxicity. In the rabbit study, a NOAEL of 5 mg/kg bw/day was established for maternal toxicity (maternal toxicity was observed at 5 mg/kg bw/day, but was minimal and not statistically significant and comparable to that of the xylene control group); a dose of 25 mg/kg bw/day was determined to be the NOAEL level for fetal toxicity. Due to the low quality of the latter study this NOAEL-value is not brought forward to the risk assessment.

Genotoxicity

DCOIT produced no evidence of genotoxicity when tested in a battery of *in vitro* and *in vivo* tests. NNOMA metabolite was not mutagenic in a bacterial mutation test.

Chronic toxicitiy/ carcinogenicity

Chronic toxicity and carcinogenic potential of DCOIT has not been tested. Waving of a long-term study has been justified by the Applicant based on the existing information on genotoxicity of DCOIT, the toxic profile of DCOIT seen in the repeated dose studies and comparison with structurally related isothiazolones.

A common feature of the repeat dose studies is that irrespective of the species or the route of administration the major toxicity observed is irritation/corrosion at the site of primary contact. In none of the studies was there any significant systemic toxicity. Doses or concentrations that may induce systemic toxicity seem to be higher than the concentrations that induce significant local toxicity due to irritation, thus hindering the evaluation of systemic toxicity. In addition, there is no evidence that either DCOIT or its metabolites bioaccumulate. Genotoxicity studies on DCOIT were negative, both *in-vitro* and *in-vivo*, thus arguing against a potential genotoxic

mechanism of carcinogenesis. Furthermore, no evidence suggestive of an endocrine mechanism of carcinogenesis has been reported in the repeated dose studies. Potential tumour promoting effects caused by chronic tissue irritation will only be relevant if long-term exposure occurs to DCOIT concentrations that gives rise to local toxicity.

The probable lack of carcinogenicity of DCOIT can be supported by consideration of chronic studies performed on three structurally related isothiazolinones; 5-chloro-2-methyl-2H-isothiazolin-3-one (CMI), 2-methyl-2H-isothiazolin-3-one (MI), and 2-Octyl-3(2H)-isothiazolone (OIT). Neither of these carcinogenicity studies indicates a carcinogenic potential.

Neurotoxicity

No neurotoxicity studies are reported, and the toxicological information does not indicate that DCOIT has neurotoxic properties. In addition to the lack of evidence pertaining to neurotoxicity, the structure of DCOIT does not contain any structural alerts for neurotoxicity.

Human data

Clinical irritation and sensitization trials were performed in humans in the late 1980s and the early 1990s in the United States. DCOIT Technical was neither irritating nor sensitizing to the skin of humans in petrolatum or corn oil at concentrations up to and including 1000 ppm a.i.

Studies of DCOIT Technical in ethanol demonstrated that 250 ppm - 350 ppm a.i. (0.025-0.035%) is at or near the threshold concentration for irritation and sensitization in humans.

Converting this to a dose per area of exposed skin gives a LOAEC for irritation of approximately 7µg/cm^2 for DCOIT in ethanol. Extrapolating from a LOAEC to a NOAEC leads to a NOAEC of approximately 0.01%, equivalent to a dose of about 2.3 µg/cm^2, for local skin irritation following exposure to DCOIT in ethanol. The threshold dose for irritation appears to be considerably higher ($\geq$ 50 µg/cm^2) for DCOIT diluted in petrolatum or corn oil.

The human patch test of DCOIT in ethanol was selected for the risk assessment of local skin effects (irritation).

In conclusion, the primary human health hazards associated with DCOIT are irritation of the skin, eyes, intestinal tract or lungs (i.e. sites of first contact), as well as sensitisation following repeated skin contact. Local effects are seen both in single dose studies, sensitisation studies and in repeated dose studies. There is no evidence of significant systemic toxicity at doses below those that gives significant local irritation.

2.2.1.2 Hazard identification and effect assessment of the product

Two products were included as representative formulations in the CA-report, a theoretical product containing 3% DCOIT (an antifouling paint incorporating a preformulation of DCOIT in xylene) and a real product containing approximately 2% DCOIT (Antifouling Globic 81900).

Studies were conducted on the preformulation (C-9211 HQ, commercial product called Sea-Nine™ 211 Antifouling Agent containing approximately 30% DCOIT in xylene) and on the paint formulation Antifouling Globic 81900.

No specific dermal absorption study was conducted with SEA-NINE™ 211 Antifouling Agent. However, a high penetration of DCOIT dissolved in acetone or DPGME into the skin of rats has been shown (see 2.2.1.1).

Two *in vitro* percutaneous absorption studies of DCOIT from antifouling paint formulations were performed. The results obtained from these two studies indicate that the absorption of DCOIT in a paint formulation through human epidermis is low when compared with the absorption of DCOIT in the preformulations. An antifouling paint formulation contains high concentration of solids, polymer and a non-polar solvent. DCOIT has seemingly a tendency to partition preferably in the non-polar media and to remain adsorb into the solid particles and polymer. Thus, the amount coming into direct contact with the skin and being available for skin uptake is reduced.

One of the formulations tested was equivalent with Antifouling Globic 81900. In the study the mean absorption rate over the entire 24 h exposure period was 0.405 $\mu g/cm^2/h$, with the total amount of DCOIT absorbed through human skin by 24 h being 10.2 $\mu g/cm^2$ (equivalent to 2.89% of the applied dose). In rat, the mean absorption rate over the 24 h period was 2.91$\mu g/cm^2/h$, with the total amount of DCOIT absorbed through rat skin by the end of the exposure period being 70.9 $\mu g/cm^2$ (equivalent to 20.1% of the applied dose). Since it was not possible to remove the test substance properly from the skin surface after exposure, and tape stripping was not performed, the unabsorbed dose and the dose remaining in the skin were not separated. Thus no estimate could be made on how much of the substance remaining in the skin was potentially available for absorption.

Of that reason a second *in vitro* study on the absorption of DCOIT through human skin from a different antifouling paint formulation containing 2.6% (w/w) DCOIT was included in the report. In this study, the mean maximal flux for the absorption of DCOIT was 0.208 $\mu g/cm^2$/hour, with the total amount of DCOIT absorbed by 24 h being 1.1% of the applied dose. The amount in the skin was 0.9% (including all, but the first 5 tape strips). Hence, the absorbable dose was approximately 2%.

If one assumes that the percentage of DCOIT retaining in skin is similar to the absorbed dose not only for this antifouling paint formulation, but also for the Antifouling Globic 81900, one can derive an absorbable dose value of approximately 6% for the latter formulation. This value was used in the risk assessment for both Antifouling Globic 81900 and the theoretical product).

As the dermal penetration of DCOIT is highly formulation-dependent, studies on the actual formulations or argumentation for read across from related formulations should be provided in the product authorisation.

Acute oral, dermal and inhalation toxicity studies with the preformulation SEA-NINE™ 211 have been performed. The preformulation is of low toxicity by ingestion or dermal exposure (LD_{50} > 2000 mg/kg). However, the preformulation is very toxic by inhalation with LC_{50} values of 0.22 mg/L, thus warranting a classification of the preformulation as very toxic by inhalation (T+; R26).

Acute oral and dermal toxicity studies have been performed with an antifouling paint formulation (Antifouling Globic 81900). Oral and dermal LD_{50} values were above 5000 mg/kg bw and 2000 mg/kg bw, respectively, and thus do not warrant classification. The inhalation toxicity study was waived, but a classification for this endpoint is suggested based on the product components.

A classification of the SEA-NINE^{TM} 211 preformulation as corrosive to skin and eye (C; R34) is proposed. Furthermore, the preformulation should be considered as respiratory irritants (Xi; R37).

Setting lower specific concentration limits for corrosion/irritation should be considered for the active substance. No specific proposal has been made, but based on the available data, the lower limit for classification for irritation should be well below 1%. Hence, the presence of 3% DCOIT in an antifouling paint would trigger the classification of the paint, even without other constituents with corrosive/irritative properties unless the product is tested and shown not to be an irritant.

The paint formulation Antifouling Globic 81900 does not warrant classification for skin irritation. However, it should be classified for eye irritation according to the criteria in the CLP regulation due to the corneal opacity response and the lack of complete reversibility during the post-exposure period. There is no test information on respiration irritation of Antifouling Globic 81900.

The SEA-NINE^{TM} 211 preformulation should be classified with Xi; R43.

The presence of 3% DCOIT in an antifouling paint will trigger the classification: Xi; R43 for the paint based on the classification of the active substance in the absence of further information (general concentration limit being 1%; a lower specific concentration limit for DCOIT proposed).

The paint formulation Antifouling Globic 81900 is considered not to be a sensitizer based on a Magnusson-Kligman Maximisation Test in guinea pigs. Thus, the composition of the formulation (e.g polymers) might reduce the sensitizing effect of DCOIT, but this effect seems to be product specific.

2.2.1.3 Exposure assessment and risk characterisation

Acceptable Exposure Limits (AEL) for acute and medium term time frame for DCOIT was derived by applying a combined 100-fold assessment factor to account for potential inter-species (10x) and intra-species (10x) variation in toxic response and correcting for the low oral absorption (20%). The resulting AELs for DCOIT are as follows:

AEL $_{acute:}$ 0.04 mg/kg bw based on the 28 day oral gavage study in rats

AEL $_{medium\ term/\ long\ term:}$ 0.02 mg/kg bw/day based on the 3 month dietary study in dogs

There is no chronic study upon which a long term AEL can be based, due to a well documented waving proposal. However, as local irritation is dominating and potential adverse systemic effects seem to occur at higher doses, the Rapporteur propose that the AEL $_{long\ term}$ is set at the same level as the AEL $_{medium\ term}$ (0.02 mg/kg bw/day).

Residues of DCOIT and its metabolites in fish and other seafood might be foreseen as a result of use of antifouling paint. Hence, deriving of an Acceptable Daily Intake (ADI) and an Acute

Reference Dose (ARfD) were proposed. The same studies used for establishing the $AEL_{long\ term}$ and AEL_{acute} were proposed used, applying a 100-fold assessment factor to account for potential inter- and intra-species variation in toxic response. No correction for oral absorption was made as ADI and ARfD are external reference values.

ARfD: 0.2 mg/kg bw/day

ADI: 0.1 mg/kg bw/day

The irritant/corrosive properties of DCOIT dominate the toxic effects in the available animal experiments. Because of this, the general toxicity observed (e.g. reduced body weight) is considered secondary to local toxicity, and consequently the NOAEL that is proposed for systemic toxicity (and the AEL) is most likely too conservative.

Acceptable Exposure Concentrations (AECs) for local dermal and respiratory effects (irritation) were established for DCOIT as local toxicity is considered the critical endpoint associated with exposure to the substance.

An **AEC_{dermal}** of **0.003 % w/v** DCOIT was derived based on repeated exposure human patch tests of DCOIT in ethanol, supported by results from the 21 day dermal rabbit study on a preformulation with 35% DCOIT in mixed xylenes and the guinea pig maximation test on DCOIT Technical. Human skin in general does not seem more sensitive than animal skin based on these studies.

A dose per skin surface value of **0.7 µg DCOIT/cm^2** was derived based on the human patch tests. An assessment factor of 3.2 was applied to the NOAEC value (extrapolated from LOAEC with an assessment factor of 3, see 2.2.1.1), consisting of 1 for interspecies variation (human data used as a basis) and 3.2 for intraspecies variation.

An **$AEC_{inhalation}$** for long term exposure of **0.013 mg DCOIT/m^3** and an $AEC_{inhalation}$ for medium term exposure of 0.026 mg DCOIT/m^3 were derived based on the thirteen week nose-only inhalation study in rats on a preformulation containg 32.6% DCOIT in o-xylene.

The established NOAEC in the study (0.02 mg/m^3) is considered conservative due to the additional toxicity of xylene, and because the spacing of the two lower doses (0.02 and 0.63 mg/m^3) was large. In order to calculate a more realistic NOAEC for inhalation, the LOAEC value (0.63 mg/m^3) was used with an assessment factor of 3 to extrapolate from the LOAEC to a modified NOAEC of 0.21 mg/ m^3. An assessment factor of 16 was applied to this modified NOAEC, consisting of 2.5 for interspecies variation (disregarding the toxicokinetic component of the interspecies factor); 3.2 for intraspecies variation (minor influence of toxicokinetic factors) and 2 for extrapolation from subchronic to chronic exposure (relevant for $AEC_{inhalation\ long\ term}$ only).

The risk assessment for DCOIT in the theoretical product and the proposed risk reduction measures are based on an evaluation of systemic and local effects. A quantitative exposure assessment is made for systemic and local respiratory effects (irritation) whereas a semi-quantitative exposure assessment is made for local dermal effects.

However, the formulation of a product could have significant impact on the potential for local effects of the substance, and a local AEC based on studies on the active substance will consequently not necessarily be representative for the end use formulation. The questionable relevance of these external reference values for products has been acknowledged as one of the major short comings with the methodology for local risk assessment as described in the

current guidance document on risk characterization of local effects (ex-ECB 2010). Hence, according to a draft guidance document on risk characterization of local effects (ex-ECB 2013, guidance not yet agreed), risk characterisation for local effects should in the future as a default be qualitative.

Studies on the real product (Antifouling Globic 81900) have demonstrated that this product has a lower potential for dermal irritation than would be expected looking at the mere concentration of the active substance. Classification of the product for neither skin irritation nor sensitisation is warranted.

Consequently, as for the risk assessment of DCOIT in the paint formulation Antifouling Globic 81900 a local risk assessment for dermal irritation has not been performed. However, in lack of test information available on respiration irritation of the product, a risk assessment for local effects on the respiratory tract (irritation) has been performed using the external reference value set for the active substance, acknowledging the fact that this value is conservative. Antifouling Globic 81900 is an eye irritant, necessitating the use of eye protection.

In addition to the risk assessment for respiratory irritation, a risk assessment based on systemic effects is performed. It should be kept in mind though that the AEL used in the risk characterisation for systemic effects is based on NOAELs from repeated dose studies in which local toxicity was observed at the LOAEL dose (see above). It is thus likely that the derived AEL is too conservative for DCOIT in a non-irritating formulation.

Quantitative risk assessments were performed, comparing the estimated exposure with relevant reference values (AECs or AELs) with the desired result that the ratio (Exposure/AEL) or (Exposure/AEC) is less than 1.

For risk characterisation of systemic effects the Margin of Exposure (MOE) approach was used as well. The MOE approach compares the critical NOAEL with the estimated exposure. For the evaluation of systemic effects of DCOIT a minimum desired Margin of Exposure (ratio of the NOAEL to Exposure) of 100 is required.

Human exposure

The active substance DCOIT Technical and the pre-formulations (Sea-Nine™ 211/211N Antifouling Agent) are produced in closed processes outside Europe.

The Technical Notes for Guidance on Data Requirements for active substances and biocidal products (ex-ECB, 2000) stipulates that substances manufactured outside the EU do not need a description of the manufacturing process for exposure purposes.

Marine Antifoulant (MAF) coatings are produced by large companies in a relatively small number of plants. Exposure of plant workers during the formulation of biocidal products is not within the scope of Biocidal Products Directive and has not been addressed within this CA-report as other legislation applies (Technical meeting in the Biocides Group in December 2007, TMV07). However a description of the production of an antifoulant paint containing DCOIT is included for information.

Professional workers may be exposed during the application and removal of antifouling products containing DCOIT. Professional painters work year-round but applying antifouling products is intermittent (and episodic). The most appropriate Acceptable Exposure Limit (AEL) for use in the risk characterisation is considered to be that for exposures of medium-term duration.

The use of DCOIT is evaluated only for professional use. The only case of exposure of the general public during the paint application stage might be the potential exposure of by-stander. However, sites where application/removal of antifouling paint will be undertaken by professionals should be inaccessible to the general public.

Following application, the antifouling product may leach from treated surfaces into water and may be taken up by fish and other marine organisms leading to residues of DCOIT and its metabolites in seafood. A simplified assessment of the risk to food consumers due to contamination of fish and other seafood was undertaken.

Relevant routes of exposure are percutaneous absorption and exposure via inhalation.
The bodyweight values used in the exposure assessment are 60 kg for adults.

Table 2.4. Main path of human exposure

Exposure path	Industrial use	Professional use	General public*	Via the environment
Inhalation	Yes	Yes	No	No
Dermal	Yes	Yes	No	No
Oral	No	No	No	Yes**

** To keep unauthorised persons from entering the treatment area the product label should carry the phrase "Unprotected persons should be kept out of treatment areas".*
*** Consumption of seafood containing residues of DCOIT and its metabolites*

Human health risk for professional users (Primary exposure)

Exposure assessments were carried out on two representative formulations; a theoretical product containing 3 % DCOIT and a real product (Antifouling Globic 81900) containing 2% DCOIT (see 2.1.2).

Several scenarios were identified in which exposure is likely to occur to professionals (primary exposure)

- **spray painter** (ship hulls)
- **painter using roller and brush** (spot application)
- **painter using spray equipment or roller and brush** (other structures)
  (no separate exposure calculations performed as the exposure parameters for the tasks of spraying and using brush and roller will adequately cover this use).
- **potman** (preparing the antifoulant paint and ensuring continuous supply of paint to the high pressure pump)
- **ancillary worker** (general assistance to the applicator)
- **paint stripping worker**
- **grit filler** (assisting the sand blaster)

DCOIT-containing antifouling products are only to be applied in professional ship yards. Unless involved in the work, it is not realistic that a bystander will be present within close vicinity of the painting operations. At the Biocides Technical Meeting in October 2011, it was agreed that a specific bystander exposure scenario was not necessary to include in the CA reports on active substances in antifouling products. To keep unauthorised persons from entering the treatment area it was agreed that the product label should carry the phrase ″Unprotected persons should be kept out of treatment areas".

The exposure assessment for professional use of antifoulant paint is based on on generic exposure data. The simple database models presented in the Technical Notes for Guidance (TNsG) of Human exposure to biocidal products of 2002 (ex-ECB, 2002) as updated in the User Guidance as well as raw data behind these models, were used. Exposure data for professional use of antifouling paints which were published after the first TNsG on human exposure/User Guidance, were considered as well; i.e.:

i) exposure measurements for spray painting and mixing of antifoulant paint (Hughson and Aitken, 2004, measurements included in BEAT)
ii) exposure measurements for application (spraying and rolling) and removal of antifouling paints (sand blasting) (Links et al. 2007)

Recommendations from the Human Exposure Expert Group on the use of the latter study were taken into account (HEEG, 2012).

Results from two worker exposure studies conducted by Rohm and Haas Company in 1990 with DCOIT during antifouling paint application in an American and Danish shipyard, were included in the CA-report for information only as the data sets were small, and only stationary air sampling was undertaken.

A tiered approach was followed. Tier I assumes use of neither Personal Protective Equipment (PPE), nor Respiratory Protective Equipment (RPE). Tier II estimates for all of the scenarios assume appropriate PPE/RPE protection factors (5 or 1 % clothing penetration for single and double layer of clothing respectively and respiratory protection with an applied protection factor of 10 for disposable dust/mist mask or 40 for full face mask, HEEG, 2010) or are based on actual measurements inside gloves/protective clothing.

As for the exposure assessment based on local effects a quantitative risk assessment was performed for respiratory irritation whereas a semi-quantitative risk assessment was performed for dermal effects.

For the exposure assessment for systemic effects a dermal absorption of 100% was used in tier I for the theoretical product. In tier II 6% was used. As for the real product a dermal absorption of 6 % was used in both tiers (See further comments in 2.2.1.2)

For the theoretical product, exposure above the threshold value for systemic effects was identified for several scenarios based on the more superior/relevant exposure data, whereas the exposure was below the threshold for respiratory irritation for all scenarios, but the one for the grit filler (borderline risk; see results presented in Table 2.5).

As for dermal effects, the concentration of DCOIT in the theoretical product (3%) is far above the concentration of DCOIT that could lead to locale effects (AEC_{dermal} for dermal irritation being 0.003% and the proposed specific concentration limit for classification for sensitization 0.001% [4]. For further information see 2.2.1.1and 2.2.1.3.). As the product is a theoretical product only, any possible influence of other components in the formulation on the local effects of DCOIT is disregarded.

The comparison provides only a rough idea of the magnitude of a **possible** risk without taking into account any risk mitigation measures/personal protective equipment. However, personal protective equipment for dermal protection will not decrease the concentration of the active substance to which a worker is exposed, but rather the occurrence of skin contact. As can be seen from the referred exposure studies, some dermal contact is unavoidable when applying/removing antifouling paint despite the use of PPE/RPE (ref. measurements inside coveralls and gloves).

The external reference values are based on studies on the active substance/concentrate. The composition of an antifouling paint formulation (high concentration of solids, polymer and a non-polar solvent) seems to influence both the potential for dermal effects and the dermal penetration of the substance as was demonstrated in the studies on the real product, Antifouling Globic 81900 (see 2.2.1.2). As the product is not classified for local dermal effects (and the AEC_{dermal} is not relevant for the product), a local risk assessment for such effects was not performed.

Assuming use of appropriate protection (PPE/RPE), an estimated exposure below the threshold concentration for systemic effects ($AEL_{medium/long\ term}$) were found for all scenarios for Antifouling Globic 81900, but the ones for the ancillary workers (borderline risk) and

[4] Proposal based on animal data. A higher concentration limit has been proposed by the Applicant based on human data. To be further discussed by the Risk Assessment Committee under ECHA.

potmen. This conclusion was drawn when the exposure calculations were based on what is considered the more superior/relevant exposure data (see shaded rows in the tables with results of the risk characterisation presented in Table 2.6).

As for the ancillary worker two sets of exposure data were used as the basis for the exposure calculations. Based on the data presented in the Health and Safety Executive report (HSE-UK, 1999) which were rather limited, and assuming use of the same protective equipment as the spray painter, the estimated exposure was below the $AEL_{medium/long\ term\ exposure}$. However, based on the study by Hughson and Aitken, the estimated exposure was slightly above the threshold value. The contribution from inhalation exposure was in both cases minor compared to dermal exposure. A higher number of measurements were included in the latter study, but from one single dock only and with repeated measurements from the same individuals. Furthermore, the exposure may have been higher than in a commercial dry dock where marine vessels tend to be spray painted without enclosures. As only potential hand exposure was measured in the study, default values for glove penetration (10%) were used when converting the value to actual hand exposure. The actual permeation of DCOIT from MAF paint through gloves has been demonstrated to be much less than the default value in a permeation test. Other mechanisms for exposure exist than permeation through the glove material (e.g. exposure to contamination inside gloves due to taking on and off gloves). Nevertheless, using the default glove penetration seems to be over conservative; no risk is observed if a somewhat lower penetration of 8% is used in the exposure calculations.

As for the potmen, a risk ratio of 1.7 was observed in a refined tier II calculation, assuming the same degree of protection as the sprayer, when based on the Mixing and loading model 6 from the TNsG of Human exposure of 2002 (using indicative values proposed in the User Guidance). The contribution from inhalation exposure was minor compared to dermal exposure.

The hand exposure amounted to almost 90% of the total dermal exposure (in the refined tier II calculation). As based on measurements inside gloves, the exposure value could not be further reduced.

Exposure data from the study by Links et al (Links et al., 2007) could not be used in a refinement of the potman scenario as the assistant workers in the study apparently had the combined task of paint filling (pot man) and general assistance (ancillary worker). It is recognized though that an exposure assessment based on the exposure data for these assistant workers would have demonstrated safe use for these workers (risk ratio <1). Thus, this indicates that safe use for all workers at a dockyard can be achieved by organizational measures and appropriate use of suitable PPE/RPE.

Looking into the data set, a striking finding was the lower actual versus potential hand exposure ratio reported for antifouling paint application tasks (paint sprayer, painter using roller and assistant worker), compared to the exposure data from the HSE surveys (HSE, UK, 1999) included in the TNsG on human exposure of 2002; the actual hand exposure amounted to less than 1% of the potential hand exposure for all three tasks. Appropriate use of suitable chemical resistant long gloves, properly fitted with the coverall and changed after each working shift, if needed is important to reduce the hand in glove exposure.

An acceptable risk to the potman needs to be demonstrated at the product authorisation stage.

It should be kept in mind that the AEL used in the risk characterisation for systemic effects is based on NOAELs from repeated dose studies in which local toxicity was observed at the

LOAEL dose. It is thus likely that the derived AEL is too conservative for DCOIT in a non-irritating formulation.

A comparison of the predicted external exposure concentration of DCOIT in air with the $AEC_{inhalation}$ demonstrated that RPE with an assumed protection factor of 40 is needed to protect from local effects for the spray painter, the paint stripper and the grit filler. As for ancillary workers and potmen a facial mask with an assumed protection factor of 10 seems adequate to protect from local respiratory effects. The estimated inhalation exposure is below the threshold value even without use of RPE for the painter using brush and roll (see table with results in Table 2.5 and Table 2.6).

The risk of local effects on skin, eyes and respiratory tract (sensitization and/or irritation) as well as potential systemic effects from DCOIT must be controlled through the use of suitable risk management measures, including process optimisation, engineering control and appropriate and suitable PPE/RPE.

The contamination of outer (and inner) gloves was demonstrated to be high for several tasks. Appropriate use of suitable chemical resistant gloves (nitrile rubber gloves or equivalent, properly fitted with the coverall) is hence important to reduce exposure. The permeation of DCOIT from antifouling paint through nitrile rubber gloves and Hot mills cotton triple layer glove have been tested and shown to be below 0.2 %. However, permeation through the glove material is not the only mechanism for hand exposure, and care should be taken to avoid compromising the barrier function of the glove, contaminating the inside of gloves when taking on and off gloves etc. The gloves should be disposed regularly.

Based on the risk assessment of the real product, Antifouling Globic 81900, a double coverall with a chemical resistant outer layer with a hood worn over a cotton coverall of a contrasting colour to the product being applied should be used for paint sprayers, ancillary workers, potmen, paint strippers and grit fillers. The outer coverall should be discarded after each spray session/working day whereas the inner coverall should be changed regularly and on signs of breakthrough. A single layer coverall of impermeable material seems to give sufficient protection for painters using roller and brush only.

Respiratory protective equipment (RPE) with an assumed protection factor of at least 40 is required for paint sprayers, paint strippers and grit fillers. As the ancillary workers work in close collaboration with the sprayer the same respiratory protection as for sprayer might seem resonable as well. This RPE should provide head and face protection. Disposable RPE with an assumed protection factor of at least 10 is required for painters using roller and brush and potmen. The need for RPE should be informed by a suitable risk assessment.

Antifouling Globic 81900 is an eye irritant, necessitating the use of eye protection.

Feet exposure could be reduced by appropriate use of adequate and suitable impermeable boots or boots protection associated with impermeable coverall properly fitted with the coverall.

PPE should be removed and replaced immediately if there is any indication of degradation or chemical breakthrough. It should always be regarded as the `last resort' to protect against exposure to biocides. The provision of appropriate engineering controls and safe systems of work should always be considered first.

Training in correct use, removal and storage of PPE/RPE and establishing a routine for regular replacement of contaminated PPE/RPE is needed.

A system of health surveillance (i.e. regular skin inspection and recording, by a trained individual) is expected to be in place where sensitising products are regularly used.

Human health risk for the general public - Indirect exposure via the environment

A simplified assessment of the risk to food consumers due to contamination of fish and other seafood was undertaken based on the predicted environmental concentration (PEC) of DCOIT in fish/shellfish (reflects the sum of parent DCOIT and its metabolites) and the proposed Acceptable Daily Intake (ADI) for DCOIT.

Based on the highest predicted PECs for fish and invertebrates (theoretical product, commercial harbours, new building / maintenance and repair and in use phase, assuming a 20 % market share for DCOIT) and an assumption that DCOIT is the most toxic substance, a 15 kg child would have to consume 32 kg and an adult 128 kg fish a day to exceed the ADI. Even higher quantities would have to be consumed of shellfish to reach the ADI. Hence, a risk to consumers from consumption of fish and other seafood contaminated by DCOIT is not expected.

Table 2.5: Risk Characterisation for professional use of a theoretical paint

User Group	Ref	Tier	PPE [a]	RPE [b]	Inhalation intake (mg/kg bw day)	Dermal uptake (mg/kg bw day)	Total systemic uptake (mg/kg bw day)	MOE	Exposure/ AEL [c]	Inhalation mg/m³	Exposure/ AEC [d]
Spray painter	1	I	-	-	3.32 E-02	33.9	**34.0**	**0.059**	**1.7E+03**	**0.52**	**20**
		II	D	40	8.29E-04	0.025	**0.026**	77	**1.3**	0.013	0.50
Painter using brush and roller	2	I	-	-	4.7 E-05	4.83	**4.83**	**0.41**	**242**	1.5E-03	0.058
		II	S	10	4.7 E-06	0.054	**0.054**	**36.8**	**3**	1.5E-04	0.0058
	Refinement										
	6	I	-	-	2.6 E-04	7.49	**7.5**	**0.27**	**375[e]**	8.4E-03	0.32
		IIb	S	10	2.6 E-05	0.00119	0.0012	1651	0.06[e]	8.4E-04	0.032
Pot-man	3	I	-	-	3.6E-03	11	**11**	**0.18**	**561**	**0.057**	**2.2**
		II	S	10	3.6E-04	0.071	**0.071**	**28.2**	**4**	0.0057	0.22
		IIalt	D	40	9.1E-05	0.050	**0.050**	**39.7**	**3**	0.0014	0.054
Ancil-lary worker	4	I	-*	-	9.2E-03	5.59 *	**5.60**	**0.36**	**280**	**0.14**	**5.4**
		II	S	10	9.2E-04	0.033	**0.033**	**60**	**1.7**	0.014	0.54
		IIalt	D	40	2.3E-04	0.020	0.020	100	1.0	0.0036	0.14
	5	I	-	-	2.15E-02	11.5	**11.5**	**0.17**	**575**	**0.34**	**13**
		II	S	10	2.15E-03	0.050	**0.052**	**38.3**	**3**	**0.034**	**1.3**
		IIalt	D	40	5.33E-04	0.035	**0.036**	**56**	**1.8**	0.0084	0.32
Paint stripper	1	I	-	-	1.31E-02	8.40	**8.4**	**0.24**	**421**	**0.21**	**8.1**
		II	D	40	3.27E-04	0.0066	0.0070	287	0.3	0.0052	0.20
	Refinement										
	6	I	-	-	3.10E-02	3.89	**3.9**	**0.51**	**196[e]**	**0.50**	**19**
		IIb	D	40	7.7E-04	0.029	**0.030**	**68**	**1.48[e]**	0.012	0.46
Grit filler	6	I	-	-	7.16E-02	13.8	**13.8**	**0.14**	**692**	**1.1**	**42**
		II	S	10	7.16E-03	0.0250	**0.032**	**62**	**1.6**	**0.11**	**4.2**
		IIalt	D	40	1.79E-03	0.0096	0.0114	175	0.6	**0.029**	**1.1**

Table 2.6: Risk Characterisation for professional use of Antifouling Globic 81900 (Systemic and local respiratory effects)

User Group	Ref	Tier	PPE [a]	RPE [b]	Inhalation intake	Dermal uptake	Total systemic uptake	MOE	Exposure/ AEL [c]	Inhalation	Exposure/ AEC [d]
					(mg/kg$_{bw}$/day)					mg/m^3	
Spray painter	1	I	-	-	2.2E-02	1.36	**1.38**	**1.4**	**69**	**0.35**	**13**
		II	D	40	5.5E-04	1.7E-02	1.7E-02	116	0.86	0.0087	0.33
Painter using brush and roller	2	I	-	-	3.1E-05	0.19	**0.19**	**10**	**9.7**	0.001	**0.038**
		II	S	10	3.1E-06	0.036	**0.036**	**55**	**1.8**	0.0001	0.0038
	Refinement										
	6	I	-	-	1.8E-04	0.30	**0.30**	**6.7**	**15**[e]	0.006	0.23
		IIb	S	10	1.8E-05	7.9E-04	8.1E-04	2476	0.040[e]	0.0006	0.023
Pot-man	3	I	-	-	2.4E-03	0.45	**0.45**	**4.4**	**23**	**0.038**	**1.5**
		II	S	10	2.4E-04	0.047	**0.047**	**42**	**2.4**	0.0038	0.15
		IIalt	D	40	6.1E-05	0.034	**0.034**	**59**	**1.7**	0.00095	0.035
Ancil-lary worker	4	I	-	-	6.1E-03	1.32	**1.32**	**1.5**	**66**	**0.096**	**3.7**
		II	S	10	6.1E-04	2.2E-02	**2.2E-02**	**90**	**1.1**	0.0096	0.37
		IIalt	D	40	1.5E-04	1.3E-02	1.3E-02	150	0.7	0.0024	0.092
	5	I	-	-	1.4E-02	0.46	**0.47**	**4.2**	**24**	**0.22**	**8.5**
		II	S	10	1.4E-03	3.3E-02	**3.5E-02**	**57**	**1.7**	0.022	0.85
		IIalt	D	40	3.5E-04	2.3E-02	**2.4E-02**	**84**	**1.2**	0.0055	0.21
Paint stripper	1	I	-	-	9.1E-03	3.5E-01	**3.6E-01**	**5.6**	**18**	**0.15**	**5.8**
		II	D	40	2.3E-04	4.6E-03	4.8E-03	413	0.24	0.0037	0.14
	Refinement										
	6	I	-	-	2.2E-02	1.6E-01	**1.8E-01**	**11**	**9.2**[e]	**0.34**	**13**
		IIb	D	40	5.4E-04	2.0E-02	**2.1E-02**	**97**	**1.0**[e]	0.0086	0.33
Grit filler	6	I	-	-	0.050	0.58	**0.63**	**3.2**	**32**	**0.81**	**31**
		II	S	10	0.0050	0.018	**0.023**	**88**	**1.1**	**0.081**	**3.1**
		IIalt	D	40	0.0013	0.0068	0.0080	250	0.40	0.020	0.77

Explanations to the tables on risk characterisation:

[a] ***PPE***:
S = Gloves, single layer coverall
D = Gloves, Double layer coveral,
APF for PPE (used when only exposure on the outer clothing, i.e. potential exposure, was measured):
Double layer coverall: 100 (1% penetration)
Single layer coverall: 20 (5% penetration)
**Gloves used also in tier I*

[b] ***RPE***: *Values given are Applied protection factor (APF) for RPE*

Dermal absorption *used in the exposure assessment:*
Theoretical product: Tier I:100 %, tier II: 6%
Antifouling Globic 81900: Tier I and II: 6%

Values in bold
[c] *exceeding the AEL medium/longterm of 0.02mg/kg bw/day*
[d] *exceeding AEC inhalation medium term of 0.026 mg/m^3*
[e]*Exposure calculation based on conservative 90th percentile values pending the establishment of 75 th percentile values (HEEG, 2012)*

References:
1. *ECB, 2002;TNsG on human exposure (Spraying model 3)*
2. *ECB 2002: TNsG on human exposure (Consumer prod. paint. model 4)*
3. *ECB 2002, TNsG on human exposure (M&L model 6)*
4. *HSE-UK, 1999*
5. *Hughson et Aitken (BEAT)*
6. *Links et al. 2007*

2.2.2 Environmental risk assessment

2.2.2.1 Fate and distribution in the environment

Abiotic degradation

The abiotic degradation kinetics for DCOIT are moderate and significantly slower than the biotic kinetics. The extrapolated hydrolysis half-life at the marine pH of 8 and default temperature of 9 ^{o}C is 148 days. No metabolites were formed in amounts > 10 % at environmentally relevant pH and temperature in the hydrolysis study. The half-life from an aqueous photolysis study was 48 days at 9 °C and pH 7. In this study, the major metabolite was N-(n-octyl) oxamic acid, formed in an amount of 31 %. Thus the primary route of dissipation of DCOIT in the environment is biological. In the troposphere, the calculated radical catalyzed degradation of DCOIT and its metabolites is very rapid resulting in half-lives of 24.4 hours or less.

Biodegradation

Results from a test on ready biodegradation showed that DCOIT was not readily biodegradable in this test. However, due to its biocidal nature, DCOIT is not suitable for testing under standard ready biodegradation protocols and inhibited the microorganisms in the test. Biodegradation simulation tests in estuarine water, water-sediment and soil microcosms demonstrated that dissipation of DCOIT from the test systems is rapid. Dissipation half-lives are 16.5 hours for freshwater, 4.08 hours in freshwater sediment and 4.7 days in soil. All values are related to a temperature of 12 °C. In the marine environment dissipation half-lives for seawater are 14 hours for coastal and estuary environments and 42 hours for distant marine environments. Half-lives in marine sediment are 3.6 hours for coastal and estuary environments and 10.8 hours for distant marine environments. The values for the marine environment are related to a temperature of 9 °C. The seawater-sediment studies have deficiencies but can be accepted nevertheless because all simulation studies together provide a consistent result regarding the half-lives of DCOIT. DCOIT is quickly removed from the aquatic environment and transformed into less toxic metabolites.

Dissipation consists of mineralization, primary degradation, chemical reaction and adsorption to organic matter.

- CO_2 development in the water-sediment studies was between 6 and 22 % of applied radioactivity. In the freshwater-sediment studies, 5-11 % CO_2 was measured after 101 days. In the seawater-sediment studies, 10-20 % (aerobic) and 7-8 % (anaerobic) CO_2 was detected at study termination. In the soil study, 11-21 % CO_2 had evolved after 30 days. In the estuarine water study, no CO_2 evolution was observed within 6 days. However, N-(n-octyl) oxamic acid (NNOOA) was formed as a major metabolite and this must involve the liberation of $^{14}CO_2$.
- Metabolism involves cleavage of the isothiazolone ring. The major metabolites formed were N-(n-octyl) malonamic acid (NNOMA; max 16 % in sediment), N-(n-octyl) acetamide (NNOA; max. 12 % in sediment), N-(n-octyl) oxamic acid (NNOOA; max. 24 % in surface water) and 2-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid) (max. 12 % in surface water at 100 ppb dosing level). 1-chloro-2-(n-octylcarbamoyl)-1-ethene

sulfonic acid was only formed at a maximum amount of 8.9 % in the estuarine study; however, concentrations were still increasing at the end of the study.

- DCOIT forms bound residues in the water-sediment and the soil studies in amounts of about 40-65% of applied radioactivity. In the estuarine water study about 50-70 % of applied ^{14}C was incorporated in a kind of biomass fraction at the end of the study.

Adsorption

In the water/sediment microcosms, DCOIT and its metabolites are rapidly partitioned into the sediment. DCOIT and its metabolites bind tightly to sediment and soil. The adsorption K_{oc} in soil range from 5659 to 25237 (mean value 12169) and from 17232 to 28320 in aquatic sediment. For sediment, the highest Koc (tested at the lowest concentration) is used for the marine risk assessment. Lack of mobility can not only be assumed for DCOIT but also for the metabolites,due to the fact that no radioactivity is found below the first 6 cm of the column and in the leachate. Due to the rapid biodegradation of parent, it is likely that only its metabolites are incorporated into the bound sediment residue, probably due to nucleophilic reaction of organic matter with reactive intermediate degradation products of DCOIT.

Bioconcentration

Bioconcentration of DCOIT was studied in several aquatic organisms. Based on analysis of total ^{14}C-residues (DCOIT + degradation/metabolism products), the steady-state BCF for bluegill sunfish (whole body) is estimated to be 750 ($K_{uptake}/K_{depuration}$). The ^{14}C-activity is primarily a cysteine adduct with a ring cleaved DCOIT metabolite. Only 1 % of the detected radioactivity in fish was DCOIT. The ^{14}C-BCF values calculated for fish are quite high for a compound with a log K_{ow} of 2.8, and the depuration rate is slow. The latter could be seen in relation to the fact that metabolites of the active compound seem to be incorporated into protein of the fish via amino acid adducts. DCOIT adsorbs rapidly to organic matter and, in simulation tests, rapidly biodegrades in the environment. Therefore, under field conditions it is not anticipated that DCOIT would have an unacceptable impact on fish.

The highest estimated kinetic BCF for DCOIT in oyster based on total ^{14}C-residues is 44. However, as the steady state for uptake was not reached in this study, no definite conclusion can be drawn on the values for BCF for invertebrates.

2.2.2.2 Environmental effects assessment

Aquatic toxicity (incl. sediment)

Acute and long-term tests are available with freshwater and marine species. The most sensitive species is *Navicula pelliculosa with a* 24 h E_rC_{50} of 1.6 µg/L and a NOE_rC of 0.34 µg/L. Chronic toxicity of DCOIT to aquatic organisms is not substantially greater than acute toxicity (i.e. acute-to-chronic toxicity ratios are <10). The freshwater PNEC is derived from this NOEC, applying an AF of 10. **$PNEC_{freshwater}$ = 0.034 µg a.i./L.** The marine PNEC is derived from the same study using an AF of 50. **$PNEC_{seawater}$ = 0.0068 µg a.i./L.**

Acute and long-term tests with freshwater and marine sediment dwelling organisms are available. Results from a chronic toxicity test with *Chironomus riparius* in artificial sediment resulted in a 10 day NOEC of 3.09 mg a.i./kg dwt (4.9 mg ^{14}C equiv./kg dwt). The 28 day NOEC from a test with the marine amphipod *Leptocheirus plumulosus* in natural sediment is 0.1 mg a.i./kg dwt (10 mg ^{14}C equiv/kg dwt). Biodegradation of DCOIT in the natural system was considerably faster than in the artificial system, showing that toxicity of the metabolites towards sediment organisms is significantly lower than of DCOIT. The NOEC of 4.9 mg ^{14}C equiv./kg dwt is used for PNEC derivation for freshwater sediment as biodegradation in sediment was not taken further into consideration in the freshwater risk assessment. It was converted to wet weight using a conversion factor of 1.184. This conversion factor was calculated from sediment characteristics in the study with *Chironomus riparius*. The NOEC based on total radioactivity becomes 4.14 ^{14}C equiv/kg wwt sediment and the **$PNEC_{freshwater\ sediment}$ = 0.41 mg ^{14}C equiv./kg wwt sediment.** It represents DCOIT and metabolites.

In the exposure calculations in the marine antifouling risk assessment biodegradation in sediment is taken into consideration and concentrations in marine sediment represent only DCOIT and not metabolites. Therefore, the $PNEC_{marine\ sediment}$ is derived from the lowest NOEC for parent substance of 0.1 mg a.i./kg dwt from the test with *L. plumolosus*, using an AF of 10. For conversion from dry to wet weight a conversion factor of 2.94 is used, which was calculated using measured data on sediment characteristics in the study report for the *L. plumolosus* test.

$PNEC_{marine\ sediment}$ (DCOIT) = 0.01 mg a.i./kg dwt sediment

$PNEC_{marine\ sediment}$ (DCOIT) = 0.0034 mg a.i./kg wwt sediment

An activated sludge respiration inhibition test has been conducted. DCOIT did not inhibit respiration of activated sludge by more than 25% at any concentration, resulting in a 3-hour EC_{50} > 5.7 mg a.i./L and a 3-hours EC_{15} value of 0.64 mg a.i./L. An assessment factor of 10 was used to derive the $PNEC_{STP}$ from the EC_{15}. **$PNEC_{STP}$ = 0.064 mg a.i./L**

Terrestrial toxicity

Acute terrestrial toxicity studies are available with microorganisms, earthworms and plants. In addition a long-term test with earthworm is available. The lowest NOEC is the earthworm $NOEC_{reproduction}$ of 5.0 mg a.i./kg dwt soil, based on initial concentrations. Due to the fact that DCOIT is not stable during the test, the NOEC is corrected for biodegradation using the Time Weight Average approach (equals a TWA NOEC of 3.5 mg a.i./kg dwt soil). An AF of 50 is used to derive the PNEC. **TWA $PNEC_{soil}$ = 0.07 mg a.i./kg dwt (= 0.062 mg a.i./kg wwt).**

The toxicity of DCOIT towards birds is low, with LD_{50} and LC_{50} values above the highest concentrations tested, respectively (> 3,580 mg a.i./kg bw and > 4,640 mg a.i./kg food). The lowest NOEC, from the short-term dietary study with mallard duck, was 625 mg/kg food. The $PNEC_{oral}$ for birds is derived from the LC_{50} with an AF of 3000. **$PNEC_{oral}$ (birds) > 1.55 mg a.i./kg food.** For mammals the lowest NOAEL was 10.1 mg a.i./kg bw/d from a 90-d subchronic toxicity with dogs. To derive the NOEC the NOAEL is multiplied with a conversion factor of 40. This gives a $NOEC_{mammals}$ of 404 mg a.i./kg food. To derive the $PNEC_{oral}$ for mammals an AF of 90 was used. **$PNEC_{oral}$ (mammals) = 4.49 mg a.i./kg food**

2.2.2.3 Fate and effects assessment of major metabolites

There are four major metabolites from the estuarine and water/sediment simulation studies:

- N-(n-octyl) malonamic acid – NNOMA (max 16% in sediment)
- N-(n-octyl) acetamide – NNOA (max 12% in sediment)
- N-(n-octyl) oxamic acid – NNOOA (max 24% in surface water at all conc. tested)
- 2-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid (max 12% in surface water at 100 ppb)

1-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid was not formed in amounts > 10% (max. amount 8.9%); however, concentrations of this metabolite at the 100 ppb dosing level were increasing during the course of the test, not reaching a plateau at the end of the study. It is therefore possible that this metabolite might have passed the 10% threshold if the study had been prolonged.

Exposure calculations and a risk characterisation have been carried out for NNOMA, NNOA (in sediment) and NNOOA (in aqueous phase). These metabolites were formed in significant amounts in the marine/estuarine simulation studies.

Biodegradation

NNOMA and NNOA have been determined to be readily biodegradable. 2-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid was found not to be readily biodegradable.

No biodegradation tests on NNOOA and 1-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid are available; however, due to structural similarities of NNOOA with NNOMA it can be assumed that also NNOOA is readily biodegradable and that 1-chloro-2-(n-octylcarbamoyl)-

1-ethene sulfonic acid is not readily biodegradable. (Q)SAR predictions confirm these assumptions.

Ecotoxicity

Acute studies with fish, invertebrates and algae are available for NNOMA and NNOA. These metabolites are 2-5 orders of magnitude less toxic to aquatic organisms than DCOIT. Algae are the most sensitive species. The E_rC_{50} for NNOMA was 9.70 mg/L and 11 mg/L for NNOA towards freshwater algae. The lowest acute endpoint was a 96 hours ErC_{50} of 0.47 mg/L for NNOMA towards the marine algae *S. costatum*; however, the result has to be treated with caution as there were problems with the control cultures in this test.

Regarding NNOOA and the sulfonic acids no experimental data are available. The (Q)SAR prediction for NNOOA indicates acute toxicity towards daphnids and algae of > 100 mg/L. For both the sulfonic acids it is indicated that these metabolites are about 3-4 orders of magnitude less toxic than DCOIT. However, these predictions cannot be used to draw a definite conclusion because of uncertainties in the models.

For NNOMA and NNOA PNECs for seawater were derived from E_rC_{50} values from studies with *Selenastrum capricornutum* applying an AF of 10,000, respectively. No $PNEC_{seawater}$ could be derived for NNOOA as no aquatic ecotoxicity studies are available for this metabolite. Due to the uncertainties of the (Q)SAR predictions and the structural similarity of NNOOA and NNOMA the $PNEC_{seawater}$ for NNOMA is used as a read-across for NNOOA.

Regarding sediment no ecotoxicity data are available for NNOMA and NNOA and the $PNEC_{marine\ sediment}$ for these metabolites were calculated with the equilibrium partitioning method from the $PNEC_{seawater}$.

Table 2.7: PNEC values for metabolites

Substance	Compartment	PNEC in marine environment
NNOMA	Seawater Marine sediment	0.97 µg/L 0.60 mg/kg wwt = 2.76 mg/kg dwt
NNOA	Seawater Marine sediment	1.1 µg/L 0.68 mg/kg wwt = 3.13 mg/kg dwt
NNOOA	Seawater	0.97 µg/L

2.2.2.4 Environmental exposure

For the life cycle stage "formulation of the biocidal product", no environmental risk assessment has been performed. According to the IC-14 Emission Scenario Document of the TGD, paint IV (Paints, Laquers and Varnishes Industry), no environmental exposure is expected from the production stage of the theoretical product and the real product (Antifouling Globic 81900). This is also supported by detailed information available from the four European production sites of Antifouling Globic 81900.

The relevant emission scenarios for the use of DCOIT containing products are application of paint during new building of ships, removal and application of paint during maintenance and

repair (M&R), and release of DCOIT during the service life of treated ships. Only professional handling of the products is covered by this report. The models used for calculations are assumed to be valid also for superyachts (size >25 m) and, as no specific scenario is available, for the industrial/professional painting of other objects (buoys, sluice doors and offshore structures). However, exposure calculations for these other objects have not been carried out.

The risk assessment of the theoretical product of the Applicant is based on a DCOIT concentration of 3 %, while the risk assessment of Antifouling Globic 81900 is based on an a.s. concentration of 2 %. The active substance DCOIT is in general used with another biocidal active substance (mostly copper oxide), however, the emissions of the second active ingredient to the environment are not addressed in this report.

The emissions during new building and M&R, i.e. application and removal activities, have been estimated using the guidance given in the OECD Emission Scenario Document for antifouling products (European Commission, 2004). First tier PEC values for surface water and freshly deposited sediment (suspended matter) were calculated using guidance given in the the EU Technical Guidance Document on Risk Assessment (ex-ECB, 2003). For second tier calculations, the estimated daily load calculated using the ESD for antifouling products was entered into MAMPEC version 2.5. In this way, steady-state PEC values were obtained for surface water (dissolved concentrations) and suspended matter. In line with previous TM agreements, the suspended matter concentrations are used for the sediment risk assessment in the first place.

For the theoretical product, the service life scenarios examined are the OECD-EU Commercial Harbour, OECD-EU Marina (adapted) and OECD-EU Shipping Lane, the Default Estuarine Harbour, Default Marina (adapted) and Default Open Sea, as well as the Finnish Commercial Harbour and the Finnish Shipping Lane. The two marina scenarios have been adapted to cover only the superyacht applications, since DCOIT is to be used on commercial vessels and superyachts > 25 m only. A total of 7 superyachts with a length between 26 and 50 m and 1 superyacht with a length of 50 m has been assumed. This is in line with information from ICOMIA (International Council of Marine Industry Associations) on numbers and distribution of boats in a marina, which have been discussed and agreed at TM level. For the Antifouling Globic 81900, the risk assessment covers the scenarios OECD-EU Commercial Harbour and OECD-EU Shipping Lane. The PECs have been calculated using MAMPEC v. 2.5. The leach rate used for the theoretical product is the CEPE-calculated rate of 2.47 µg/cm^2/day. For Antifouling Globic 81900, a CEPE-calculated leach rate of 2.3 µg/cm^2/day is used for the OECD-EU Commercial Harbour scenario. For the OECD-EU Shipping Lane scenario, a dynamic leach rate of 4.6 µg/cm^2/day from a field study reflecting dynamic conditions is used. Even if the PEC/PNEC ratio in the OECD-EU Marina scenario was above 1, the leach rate was not reduced by a factor of 2.9 for tier 2 calculations because the CEPE-calculated leach rate is in good agreement with the leach rates determined in (semi) field studies under static conditions.

The service life results have been calculated with a market share of 20 %, except for the adapted marina scenarios where the default market share of 90 % has been used. The market share of 20 % was proposed by the Applicant to be used as a default market share for booster biocides in general as it can be considered unrealistic that each booster biocide would have a market share of 90 %. Global and European market share data for DCOIT in PT 21 support using this figure, but not for marinas. The market shares of 90 % for the adapted marina

scenarios and 20 % for the rest of the service life scenarios are used for the decision regarding Annex I inclusion.

Combined PECs were determined for the theoretical product using the OECD-EU Commercial Harbour scenario, taking into account emission from application activities (which represent the highest emission load from new building / M&R) and emissions from in-service leaching from ships. The daily emission load from both typical and worst case application activities, calculated using the ESD for Antifouling Products, was added to the daily emission load from service life leaching. This combined daily emission load was entered into MAMPEC v. 2.5 to obtain steady-state PEC values for surface water (dissolved) and suspended matter.

For the adapted marina and commercial harbour scenarios, concentrations have been calculated for the area within a commercial harbour / marina as well as for the area surrounding a commercial harbour / marina as defined by MAMPEC. These surrounding water PECs represent the wider environment.

Regarding degradation input parameters in MAMPEC, surface water was considered as the main degrading compartment and the DT_{50} values of 42 and 14 hours for remote and coastal areas (described above) were used, respectively. Hydrolysis, photolysis and degradation in sediment were not taken into account. This has been agreed at TM level as a simplified approach for MAMPEC modelling. As no risks were identified for the waters surrounding the marinas/harbours (see chapter below), and since it has been decided at TM level that this is sufficient for proposing an Annex I inclusion of the active substance even if risks are identified within the marinas/harbours, it was not considered necessary to refine the modelling by taking into account degradation in sediment.

An exposure assessment has been carried out for the major metabolites N-(n-octyl) malonamic acid (NNOMA), N-(n-octyl) acetamide (NNOA) and N-(n-octyl) oxamic acid (NNOOA) for the theoretical product – for the combined new building/M&R and service life OECD-EU Commercial Harbour scenario. These metabolites were formed in significant amounts in the marine/estuarine simulation studies at environmentally relevant concentrations. The risk exposure assessment was only done for the relevant compartment for each metabolite, i.e. seawater for NNOOA and marine sediment for NNOA and NNOMA, respectively.

2.2.2.5 Risk characterization for the environment

Atmosphere

No risk assessment for the atmosphere has been conducted as emissions to air can be considered negligible. Emission of DCOIT to the air during application may occur through spray drift and volatilisation from paint during paint drying. However, the low vapour pressure of DCOIT, the Mackay level I modelling, estimations using the US EPA AOPWIN program as well as tests on atmospheric photodegradation show that it is highly probable that DCOIT will neither achieve significant atmospheric concentrations nor be transported through the troposphere over long distances.

Aquatic environment including sediment (suspended matter)

Surface water

Regarding the risk characterisation for surface water during new building and M&R, tier 2 calculations with MAMPEC, without the implementation of additional risk mitigation measures, the following can be concluded:

- **Theoretical product**: No risks are identified for the waters surrounding the commercial harbour. Risks are identified within the OECD-EU Commercial Harbour from application activities, both typical and worst case scenarios. From removal activities, a risk was only identified in the worst case scenario.
- **Antifouling Globic 81900**: The results are similar to those of the theoretical product; the PEC/PNEC ratios are slightly lower, but the conclusions are the same.

For the service life scenarios, the following can be concluded:

- **Theoretical product**: With a default market share of 90 %, no risks are identified for the waters surrounding the marinas. Risks are identified within the OECD-EU Marina and Default Marina scenarios (both marina scenarios are adapted to cover use on superyachts only). The PEC/PNEC ratio of 8.7 for seawater within the adapted OECD-EU Marina scenario is the highest risk quotient.

  With a market share of 20 % for the harbour and shipping lane/open sea scenarios, no risks to seawater are identified.
- **Antifouling Globic 81900**: With a market share of 20 % for the harbour and shipping lane scenarios, no risks to seawater are identified.

From the combined exposure from application activities and in-use leaching for the theoretical product, no risk was identified outside the commercial harbour (surrounding waters. A risk to seawater was identified within the OECD-EU Commercial Harbour. This is the situation both when considering typical and worst case application emissions.

Sediment (suspended matter)

The following conclusions can be drawn from the sediment (suspended matter) risk characterisation of the new building and M&R scenarios, tier 2 calculations with MAMPEC, without the implementation of additional risk mitigation measures:

- **Theoretical product:** No risks are identified for the waters surrounding the commercial harbour. Risks are identified within the OECD-EU Commercial Harbour from application activities, both typical and worst case scenarios. For removal, a risk was only identified in the worst case scenario.
- **Antifouling Globic 81900:** No risks are identified for the waters surrounding the commercial harbour. A risk is identified within the OECD-EU Commercial Harbour from worst case application and worst case removal activities. No risks were identified from the typical case scenarios.

The sediment (suspended matter) risk characterisation of the service life scenarios gives the following conclusions:

- **Theoretical product**: With a default market share of 90 % no risks are identified for the waters surrounding the marinas. Risks are identified within the OECD-EU Marina and Default Marina scenarios (both adapted to cover use on superyachts only). The PEC/PNEC ratio of 4.7 for suspended matter within the adapted OECD-EU Marina scenario is the highest risk quotient.

  With a market share of 20 % for the harbour, shipping lane and open sea scenarios, no risk to seawater is identified.
- **Antifouling Globic 81900**: No risks for sediment (suspended matter) are identified for any of the two scenarios (OECD-EU Commercial Harbour and OECD-EU Shipping Lane).

From the combined exposure from application activities and in-use leaching for the theoretical product, no risk was identified outside the commercial harbour (surrounding waters). A risk to seawater was identified within the OECD-EU Commercial Harbour. This is the situation both when considering typical and worst case application emissions.

It has been agreed at TM level that if risks to the aquatic compartment are identified within a harbour or marina, the active substance can still be proposed included on Annex I provided that no risks are identified in the waters surrounding the harbour or marina.

The results of the risk characterisation of the theoretical product are summarised in the two tables below.

Table 2.8: Summary of aquatic risk assessment for the theoretical product of the Applicant

Scenario			PEC/PNEC seawater	PEC/PNEC sediment (suspended matter)
New building and M&R, OECD-EU Commercial Harbour, tier 2	**Application, TC**[a]	Within[b]	**1.9**	1.0
		Outside[b]	0.13	< 0.1
	Removal, TC	Within	0.87	0.48
		Outside	< 0.1	< 0.1
	Application, WC[a]	Within	**8.8**	**4.8**
		Outside	0.62	0.34
	Removal, WC	Within	**6.0**	**4.9**
		Outside	0.43	0.28
In use phase Default market share adapted marina scenarios[c]: 90 % Market share all other scenarios: 20 %	**OECD-EU Marina, adapted,**	Within	**8.7**	**4.7**
		Outside	< 0.1	< 0.1
	Default Marina, adapted,	Within	**3.8**	**2.1**
		Outside	< 0.1	< 0.1
	OECD-EU Commercial Harbour	Within	0.46	0.25
		Outside	< 0.1	< 0.1
	Default Estuarine Harbour	Within	0.40	0.22
		Outside	< 0.1	< 0.1
	Finnish Commercial Harbour	Within	0.37	0.14
		Outside	< 0.1	< 0.1
	OECD-EU Shipping Lane		< 0.1	< 0.1
	Finnish Shipping Lane		< 0.1	< 0.1
	Default Open Sea		< 0.1	< 0.1
Combined M&R / new build and in use, OECD-EU Commercial Harbour [d]	**Application, TC**	Within	**2.4**	**1.3**
		Outside	0.16	< 0.1
	Application, WC	Within	**9.3**	**5.1**
		Outside	0.65	0.36

a) TC = Typical case and WC = Worst case.
b) Within and outside refer to within marina/harbour and outside marina/harbour (surrounding waters representing the wider environment).
c) Both the OECD-EU marina scenario and MAMPEC default marina scenario have been adapted to cover use on superyachts only.
d) The highest emissions from M&R / new building are caused by application activities, therefore these emissions are added to the emissions from in-service leaching in the combined assessment. The combined assessment takes into account emissions from both worst case and typical case application activities.

Table 2.9: Summary of aquatic risk assessment for Antifouling Globic 81900, 20 % market share

Scenario			PEC/PNEC seawater	PEC/PNEC susp. sediment
New building and M&R, OECD-EU Commercial Harbour, tier 2	Application, TC[a)]	Within[b)]	**1.8**	0.95
		Outside[b)]	0.12	< 0.1
	Removal, TC	Within	0.81	0.44
		Outside	< 0.1	< 0.1
	Application, WC[a)]	Within	**8.1**	**4.4**
		Outside	0.57	0.31
	Removal, WC	Within	**5.6**	**3.0**
		Outside	0.40	0.21
In use phase Market share: 20 %	OECD-EU Commercial Harbour	Within	0.43	0.23
		Outside	< 0.1	< 0.1
	OECD-EU Shipping Lane		< 0.1	< 0.1

a) TC = Typical case and WC = Worst case.
b) Within and outside refer to within harbour and outside harbour (surrounding waters representing the wider environment).

Risk characterisation of the surrounding waters of harbours and marinas

No risks are identified for the surrounding waters (as described in the MAMPEC v. 2.5 help notes) of the harbour and adapted marina scenarios for either Antifouling Globic 81900 or the theoretical product.

Ground water

DCOIT has a mean Koc in soil of 12169 L/kg and a soil DT_{50} of 4.7 days. Therefore, groundwater contamination is not considered likely. A ground water risk assessment has not been conducted.

Terrestrial environment

Based on the current proposed uses on large marine-going vessels the standard OECD ESD assumes that no exposure to the terrestrial environment via STP is expected to occur from the professional use of DCOIT in antifouling products and therefore, no soil risk assessment has been carried out.

Secondary poisoning risk assessment

DCOIT is not classified with very toxic (T+), toxic (T) or harmful (Xn) with at least one of the risk phrases R48, R60, R61, R62, R63 or R64 nor are there other indications (e.g.) endocrine disruption. The steady-state BCF for bluegill sunfish (whole body) is estimated to be 750 ($K_{uptake}/K_{depuration}$). This BCF was used for the secondary poisoning risk assessment of fish. A ^{14}C-BCF of 44 is used for the invertebrate assessment.

The PEC taking into account combined emissions from worst case application and in use leaching for the theoretical product, was used for the secondary poisoning assessment. No risks were identified (all PEC/PNEC ratios are < 0.1).

Metabolites

In the evaluation of the theoretical product exposure calculations and a risk characterisation has been carried out for N-(n-octyl) malonamic acid (NNOMA), N-(n-octyl) acetamide (NNOA) and N-(n-octyl) oxamic acid (NNOOA), using MAMPEC vs. 2.5. These metabolites were formed in significant amounts (> 10 %) in the marine/estuarine simulation studies at environmentally relevant concentrations. The risk characterisation was only done for the relevant compartment for each metabolite, i.e. seawater for NNOOA and marine sediment for NNOA and NNOMA, respectively. Calculations have been done for the worst case combined M&R and service life scenario (worst case in this context means worst case application plus service life using a 20 % market share)

All metabolite PEC/PNEC ratios are below 0.1.

2.2.2.6 PBT and Endocrine Effects Assessment

PBT

DCOIT does not fulfill the PBT/vPvB criteria and can therefore not be considered a PBT/vPvB substance.

- It fulfills the T-criterion based on the lowest aquatic NOEC of 0.34 µg/L.
- However, it does not meet the trigger value for BCF > 2000 for B or > 5000 for vB, as the steady state BCF based on total radioactivity is 750. The highest recorded total residue BCF was 1,300 (viscera). The B/vB-criterion is therefore not fulfilled.
- Regarding persistency DCOIT rapidly biodegrades primarily in aquatic simulation tests with a half-life of 1.6 days in surface water at 12°C. None of the major metabolites can be considered persistent. The half-live based on primary degradation in soil is 4.7 days and there is no indication that persistent metabolites have been formed. This is shorter than 120 days which is the trigger value for the P-criterion under the new REACH legislation. DCOIT does therefore not fulfill the P/vP-criterion.

Endocrine effects

Neither DCOIT nor other isothiazolinones are included in the EU list of potential endocrine disruptors (COM DG ENV, 2000).

2.2.2.7 Monitoring data

Monitoring data from several marinas and commercial harbours are available. In most samples (seawater and sediment) DCOIT (Sea-nine 211) was not detected.

It was detected in 1 out of 11 sites in the marina of Patras, however, only in 1 of 8 samples at one sampling time. A concentration of 49 ng/L was reported for seawater in August 2000 when the activity of pleasure craft vessels was the highest. This does not seem to be logical as DCOIT containing products are not intended to be used on pleasure boats. Possible explanations for this might be experimental mistakes or painting of a couple of superyachts at this point in time.

Sea-nine 211 was also detected in four sites (ports and marinas in Spain) at high concentrations relatively constant for all sites (around 3 µg/L), but only for one month. These results might be questionable because the levels reported in water (3 µg/L) are higher than the value reported at the immediate vicinity of a freshly painted boats in Denmark, which was about 0.3 µg/L. Moreover, the same concentrations are reported for harbours and marinas. As DCOIT is used almost exclusively for commercial boats, concentrations in marinas could be expected to be considerably lower compared to concentrations in commercial harbours.

The maximum concentration reported for sediment was 4 µg/kg (one study in Spain).

2.2.2.8 Risk mitigation measures

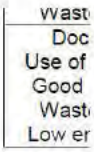
Shipyards in the EU/EEA where ships are built, maintained and repaired are subject to both national and international regulations and codes of conduct in addition to other environmental legislation that address pollution control issues. The effect of these measures depends on both the measure itself and its efficiency, and the national authorities' enforcement of the regulations.

At TM II 2011, the results of a survey made by the Community of European Shipyards Associations (CESA) on risk mitigation measures in European shipyards were presented, together with a statement from the European Council of the Paint, Printing Ink and Artists' Colours Industry (CEPE). The goal of this work was the establishment of a list of measures applicable to each scenario and a quantified protective effect of each measure. At TM IV 2011, it was agreed that it may be considered to recommend these risk mitigation measures generally for all antifoulings, and that they can be used quantitatively if needed. These general risk mitigation measures for antifouling biocides include:

- Implementation of a specific area for paint application with hard standing (yachts)
- Shrouding: protection of the application area with plastic foils and/or fine meshed nets (yachts and commercial ships)
- Thorough cleaning of dock floor with collection of solids and wastewater (yachts and commercial ships)
- Good spraying practices: Good maintenance and control of sprayers by trained people, taking into account wind speed (professional application to yachts and commercial ships)

- Wastewater collection and pre-treatment: Oil and solids separators, settling tanks, elimination of solid wastes as dangerous wastes (yachts and commercial ships)
- Low emission paint removal techniques (wet blasting associated with recycling of grit (professional yachts and commercial ships).

The CEPE statement recommends using the following reduction factors for a quantitative assessment of the application risk mitigation measures:



If the emissions from typical case application activities (on a dock, compared to worst case application on slipway) of the theoretical product within an OECD-EU Commercial Harbour are reduced by the factors representing dock floor discipline (0.75) and dock floor discipline, use of containment and good spraying practices (0.425), the following PEC/PNEC ratios are derived:

Table 2.10: Example of quantification of risk mitigation measures for application activities in a commercial harbour

Scenario: OECD-EU Commercial Harbour, within harbour (MAMPEC modelling)	**Risk reduction factor**	**PEC/PNEC seawater** [b]	**PEC/PNEC sediment (suspended matter)**
New building and M&R, Application, TC[a]	0.75	**1.4** **(1.9)**	0.77 (1.0)
	0.425	0.80 **(1.9)**	0.44 (1.0)
Combined M&R / new build and in use, In use emissions + application, TC	0.75	**1.8** **(2.4)**	0.96 **(1.3)**
	0.425	1.0 **(2.4)**	0.55 **(1.3)**

a) TC = typical case
b) The PEC/PNEC ratios from table 2.6, i.e. without having taken risk mitigation measures into account, are given in brackets for comparison.

This example, which is calculated for illustrative purposes only, indicates that appropriate risk mitigation measures could mitigate the identified risks for the application of DCOIT-containing MAFs within a harbour.

During the in-use phase of antifouling products a risk to seawater and sediment (suspended matter) was identified in the OECD-EU Marina scenario (adapted to cover use on superyachts only). Reducing this risk can only be addressed at production authorisation stage by e.g. demonstrating reduced leaching from the products. Another possible risk mitigation measure could be the restriction of the use of antifouling products in especially sensitive areas. Local authorities might enforce restrictions when establishing marinas in those areas.

2.2.2.9 Compliance with the environmental criteria for approval of active substance according to Annex VI of Directive 98/8/EC

The approval criteria of Annex VI of Directive 98/8/EC are further explained in Technical Notes for Guidance on Annex I Inclusion.

The PEC/PNEC ratios used to evaluate the compliance with the environmental criteria are as described above in chapters 2.2.2.4 and 2.2.2.5, i.e. the PECs are modeled using MAMPEC v.2.5, the water compartment is considered as the main degradation compartment, therefore degradation is taken into account for water but not for sediment. Additional risk mitigation measures are not taken into account here. However, they are discussed above in chapter 2.2.2.8.

<u>New building and M&R:</u>

The criteria for approval are fulfilled with respect to PEC/PNEC ratios for the following scenarios:

- Typical and worst case scenarios for application and removal in the waters surrounding the OECD-EU Commercial Harbour (the wider environment).
- Typical case scenario for removal within the OECD-EU Commercial Harbour.

The criteria for approval are, however, not fulfilled with respect to PEC/PNEC ratios for the following scenarios:

- Typical and worst case scenarios for application within the OECD-EU Commercial Harbour.
- Worst case scenario for removal within the OECD-EU Commercial Harbour.

<u>Service life:</u>

The criteria for approval are fulfilled with respect to PEC/PNEC ratios for the following scenarios:

- Theoretical product, market share 90 %: the waters surrounding the OECD-EU Marina and the Default Marina (both marina scenarios adapted to cover use on superyachts only)
- Theoretical product, market share 20 %: the waters within and surrounding the OECD-EU Commercial Harbour, Default Estuarine Harbour and Finnish Commercial

Harbour, as well as OECD-EU Shipping Lane, Finnish Shipping Lane and Default Open Sea

- Antifouling Globic 81900, market share 20 %: OECD-EU Shipping Lane and OECD-EU-Commercial Harbour (both within and surrounding the harbour)
- All in-service life scenarios for the metabolites

The criteria for approval are, however, not fulfilled respect to PEC/PNEC ratios for the following scenarios:

- Theoretical product, market share 90 %: the waters within the OECD-EU marina and Default Marina (both marina scenarios adapted to cover use on superyachts only)

Combined exposure from worst case M&R / new building and in-use emissions for the theoretical product: The criteria for approval are fulfilled with respect to PEC/PNEC ratios for the areas outside the OECD-EU Commercial Harbour, but not for the waters within the OECD-EU Commercial Harbour.

An active substance shall not be approved if its BCF based on total radioactivity is higher than 100 and it is not readily biodegradable unless it is clearly established in the risk assessment that under field conditions no unacceptable impact occurs on the viability of exposed organisms according to the proposed conditions of use. For DCOIT, the ^{14}C-BCF is 750 ($K_{uptake}/K_{depuration}$) and the substance is not readily biodegradable in a standard ready biodegradation test. However, in simulation tests, DCOIT rapidly biodegrades (primarily) in the environment and the BCF is < 2000 and is comprised of metabolites which are considered to be of less concern than the parent substance (all the metabolite PEC/PNEC ratios are < 0.1). It is therefore considered that the exclusion criteria related to bioaccumulation are not fulfilled.

DCOIT does not fulfill the PBT/vPvB criteria and can therefore not be considered a PBT/vPvB substance. While it fulfills the T-criterion based on the lowest aquatic NOEC of 0.34 µg/L, its BCF is less than 2000. Regarding persistency DCOIT rapidly biodegrades primarily with a half-life of 1.6 days in surface water and 4.7 days in soil (12°C). None of the major metabolites can be considered persistent.

3 PROPOSAL FOR THE DECISION

3.1 BACKGROUND TO THE PROPOSED DECISION

Two products have been assessed, a theoretical product containing 3% 4,5-Dichloro-2-octyl-2H-isothiazol-3-one (DCOIT) and a real product containing 2 % DCOIT.

The manner and areas of use listed were proposed and supported by data submitted by the Applicant. DCOIT-containing antifouling products presented was only for use by professionals. The objects to be protected include ship hulls of commercial vessels or superyachts (above 25 m length), buoys, sluice doors and immersed off-shore structures. The application is done by high pressure airless spraying and for spot applications (or small objects) by brush and roller. Removal of expired coating is done with abrasive media and/or high pressure water washing equipment. The risk assessment has been conducted for commercial vessels and superyachts (in adapted marina scenarios). For both products, a market share of 20 % was used for the commercial vessels. Global and European market share data for DCOIT in PT 21 support using this figure. For the adapted marina scenarios (superyachts only) a default market share of 90 % was used for calculations. The decision on the present assessment is based on the market share of 20 % (commercial vessels) and 90 % (superyachts).

Regarding human health, DCOIT causes corrosion/irritation and is a potent sensitizing agent. Local toxicity is considered the most critical endpoint associated with exposure to the substance with no evidence of significant systemic toxicity at doses below those that gives significant local irritation.

A local risk assessment (quantitative for respiratory irritation, semi-quantitative for dermal effects) has been performed for the theoretical product in addition to a systemic risk assessment. Established AEC and AEL values based on studies on the active substance/concentrate and estimates for dermal absorption were used. Based on these parameters exposure above the threshold concentration has been identified for all scenarios.

However, the composition of the antifouling paint formulation (containing high concentration of solids, polymer and a non-polar solvent) seems to influence both the potential for local effects and the dermal penetration of the substance. Studies on the real product have demonstrated that this product has a much lower potential for dermal irritation and sensitisation than would be expected looking at the mere concentration of the active substance. Hence, the AEC value set for the active substance for dermal irritation is not representative for the end use formulation, and a local risk assessment for dermal irritation has not been performed. In lack of studies/information on respiratory irritation of the product a risk assessment for local effects on the respiratory tract has been included (acknowledging the fact that the AEC value for respiratory irritation will be over conservative, as based on the active substance). In addition, a systemic risk assessment has been performed. Results obtained from two studies on dermal absorption of DCOIT from antifouling paint formulations through human epidermis suggest that the absorption of DCOIT is low when compared with the absorption of DCOIT diluted in solvent without polymer.

The human health risk assessment indicates that the risks for professional users of the real product for the exposure scenarios assessed are acceptable for all scenarios except the one for ancillary worker (borderline risk) and potman as long as suitable risk management measures are followed. These include process optimisation, engineering control and appropriate and suitable PPE/RPE. Training in correct use, removal and storage of the equipment and establishing of routines for regular replacement of contaminated equipment is needed. Acceptable risk needs to be demonstrated for the potman in the product authorisation.

For the environment, risks were identified within the adapted marinas (superyachts) as well as within the OECD-EU Commercial Harbour due to application and removal activities alone and in combination with in-use emissions from commercial vessels. These areas may need additional consideration at MS level. However, in the surrounding waters to the adapted marinas and harbours, safe use could be demonstrated. These conclusions are drawn without taking into account additional risk mitigation measures. For Annex I listing, it has been decided at TM level that a risk within the harbour/marina can be accepted as long as safe use can be demonstrated in the surrounding waters.

Due to the identified risk to surface water and sediment (suspended matter) from industrial removal and application activities of antifouling paint within the harbour scenarios, certain risk mitigation measures to prevent losses to surface water from these activities can be proposed at MS level. Examples of these measures are a.o.: Implementation of a specific area for paint application with hard standing, protection of the application area, thorough cleaning of dock floor with collection of solids and wastewater, good spraying practices, wastewater collection and pre-treatment, low emission paint removal techniques.

The in-use phase of DCOIT-containing antifouling products has been addressed using calculated leaching values. Robust and empirically derived leach rate data that is product specific have to be submitted for the risk assessment at the product authorisation stage for antifouling products.

During the in-use phase of antifouling products a risk to seawater was identified within the adapted marina scenarios using the default market share of 90 % for calculations. In the surrounding area to these marinas, safe use of DCOIT-containing antifouling products could be demonstrated. Reducing this risk in the marina can only be addressed at production authorisation stage at MS level by e.g. demonstrating reduced leaching from the products. Another possible risk mitigation measure could be the restriction of the use of antifouling products in especially sensitive areas. Local authorities might enforce restrictions when establishing marinas in those areas.

In general, assessments carried out for human health and the environment for the limited number of substances under PT21 (antifouling products) indicate unacceptable risks to certain end users and/or environmental compartments exposed to these substances. Specifically for DCOIT unacceptable risks for the human health and environment assessment were identified as outlined above. These assessments also indicate the need for risk mitigation measures for other use scenarios, such as technical controls and/or personal protective equipment, in order to protect end-users using these substances and minimise exposure of the relevant environmental compartments. It was agreed to utilise generic conditions in the approval Regulation (as outlined in Section 3.2) for all PT21 substances evaluated as part of the EU review programme for existing active substances so to reduce the risks for human health as

well as the risks to the environment from use of these substances. Additional provisions were also agreed on a case-by-case basis for substances where a specified risk to human health was identified. These additional provisions are outlined in Section 3.2. For the PT21 active substance, DCOIT, a specific risk of skin sensitisation was identified.

3.2 PROPOSED DECISION

The overall conclusion from the evaluation of 4,5-Dichloro-2-octyl-2H-isothiazol-3-one for use in product type 21 (antifouling products) is that it may be possible to issue authorisations of products containing 4,5-Dichloro-2-octyl-2H-isothiazol-3-one in accordance with the conditions laid down in Article 5(1) b), c) and d) of Directive 98/8/EC.

It is therefore proposed to approve 4,5-Dichloro-2-octyl-2H-isothiazol-3-one as an active substance for use in product type 21 (antifouling products), subject to the following specific conditions:

The active substance 4,5-Dichloro-2-octyl-2H-isothiazol-3-one as manufactured shall have a minimum purity of 950 g/kg.

The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.

Persons making products containing 4,5-Dichloro-2-octyl-2H-isothiazol-3-one available on the market for non-professional users shall make sure that the products are supplied with appropriate gloves.

Authorisations are subject to the following conditions:

(1) For industrial or professional users, safe operational procedures and appropriate organizational measures shall be established. Where exposure cannot be reduced to an acceptable level by other means, products shall be used with appropriate personal protective equipment.

(2) Labels and, where provided, instructions for use shall indicate that children shall be kept away until treated surfaces are dry.

(3) Labels and, where provided, safety data sheets of products authorised shall indicate that application, maintenance and repair activities shall be conducted within a contained area, on impermeable hard standing with bunding or on soil covered with an impermeable material to prevent losses and minimize emissions to the environment, and that any losses or waste containing 4,5-Dichloro-2-octyl-2H-isothiazol-3-one shall be collected for reuse or disposal.

(4) For products that may lead to residues in food or feed, the need to set new or to amend existing maximum residue levels (MRLs) in accordance with Regulation (EC) No 470/2009 of the European Parliament and of the Council[5] or Regulation (EC) No 396/2005 of the European Parliament and of the Council[6] shall be verified, and any appropriate risk mitigation measures shall be taken to ensure that the applicable MRLs are not exceeded.

Where an article has been treated with or intentionally incorporates one or more biocidal products containing 4,5-Dichloro-2-octyl-2H-isothiazol-3-one, and where necessary due to the possibility of skin contact as well as the release of 4,5-Dichloro-2-octyl-2H-isothiazol-3-one under normal conditions of use of the article, the person responsible for placing the article on the market shall ensure that the label provides information on the risk of skin sensitisation, as well as the information referred to in the second subparagraph of Article 58(3) of Regulation (EU) No 528/2012.

3.3 ELEMENTS TO BE TAKEN INTO ACCOUNT WHEN AUTHORISING PRODUCTS

Products containing 4,5-Dichloro-2-octyl-2H-isothiazol-3-one (DCOIT) have been evaluated for the use to control the growth and settlement of fouling organisms (microbes and higher forms of plant or animal species) on commercial vessels and superyachts.

- When authorising products, the nature of the products, including formulation type (e.g. matrix effects), concentrations of the active and non-active components within the product, must be considered. This is important since these factors could affect e.g. the leaching rate of the substances from the antifouling product, the potential for local human health effects and the dermal penetration of the substance. The reference product has not been fully evaluated for the purpose of the approval of DCOIT. At product authorisation, all relevant ingredients must be taken into account.
- The only use assessed for the purpose of the approval was the use by professional operators on commercial vessels or superyachts above 25 m. If other uses are applied for at product authorisation stage than those evaluated in this report, such uses should be carefully evaluated to ensure that safe use can be demonstrated. In particular the fact that DCOIT is a potent skin sensitizer should be taken into particular consideration when evaluating possible authorisation of Product Type 21 (PT21) products containing DCOIT

[5] Regulation (EC) No 470/2009 of the European Parliament and of the Council of 6 May 2009 laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and of the Council (OJ L 152, 16.6.2009, p. 11).

[6] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC (OJ L 70, 16.3.2005, p. 1).

for non-professional use. It should be noted that certain specific risk management measures considered appropriate for professional products may not be suitable for non-professional products. In addition, in the event that products containing DCOIT are subsequently authorised for use in non-professional antifouling products, persons making products containing DCOIT available on the market for non-professional users shall ensure that the products are supplied with appropriate gloves.

- Labels, safety data sheet and/or use instructions of products authorised for professional use have to indicate that the risk of local effects on skin, eyes and respiratory tract (sensitization and/or irritation) as well as potential systemic effects from DCOIT must be controlled. Appropriate use of suitable risk management measures, including process optimisation, engineering control and appropriate and suitable PPE/RPE (chemically resistant gloves and boots, goggles/face shield, protective clothing, and where necessary suitable respiratory equipment) has to be established.
- A system of health surveillance, regular skin inspection and recording, by a trained individual, should be in place for products being sensitizers.
- Formulation specific data on local human health effects (irritation and sensitization) is needed to demonstrate acceptable risk for professional workers.
- Acceptable risk for potmen has to be demonstrated before authorizing products (e.g. relevant product data, exposure data and/or RMM).
- As the dermal penetration of DCOIT is highly formulation-dependent, studies on the actual formulations or argumentation for read across from related formulations should be provided.
- To keep unauthorised persons from entering the treatment area, the product label should carry the phrase "Unprotected persons should be kept out of treatment areas".
- The efficacy of individual products must be demonstrated prior to product authorization at Member State level. As the efficacy of the example product only has been assessed in seawater, at product authorization additional efficacy data have to be provided for freshwater, if this use is foreseen.
- Robust and empirically derived leach rate data that is product specific have to be submitted for the risk assessment at the product authorization stage for antifouling products. If emissions from application and removal activities to the environment result in PEC/PNEC ratios above 1 within a harbour, appropriate risk mitigation measures may be considered at MS level to protect the environment.
- Unacceptable risks to seawater and marine suspended sediment from maintenance and repair activities within commercial harbours were shown at the approval stage of the active substance. In addition, for the in-use phase of antifouling products, a risk has been identified within the adapted marinas (superyachts). This should be carefully considered at the product authorisation stage of biocidal products
- When authorizing products containing DCOIT, authorities should consider the need to establish risk reduction measures to ensure safe use of these products in marinas, particularly in especially sensitive areas.

3.4 REQUIREMENT FOR FURTHER INFORMATION

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the approval of 4,5-Dichloro-2-octyl-2H-isothiazol-3-one (DCOIT).

5 batch analyses from the different production sites were submitted with the original dossier for the evaluation of DCOIT in the different product types. These data have been considered sufficient for evaluation of the relevance of the toxicological- and ecotoxicological studies submitted. However as the purity of raw material have been reported to have increased and the analyses are up to 10 years old, new 5 batch analyses from present production sites should be submitted at the latest 6 months prior to date of approval to the original Rapporteur Member State (Norway) and evaluated by the RMS. This would also be of value for establishing a reference source for future possible technical equivalence evaluation of other sources for DCOIT.

For DCOIT, no independent laboratory validation (ILV) of the analytical method for detection and identification of DCOIT in fish and shellfish is necessary at Annex I inclusion stage. However, at product authorization, if a maximum residue level (MRL) needs to be set for DCOIT an ILV might become necessary to conduct.

Regarding the analytical method for soil, a confirmatory method is needed as only two ions were validated. The missing data on the third fragment ion for the soil LC/MS method is to be provided at the latest 6 months prior to the date of approval to the original Rapporteur Member State (Norway). Alternatively, a suitable justification should be provided if a third ion cannot be identified due to the small size of the molecule.

Concerning the analytical method for fish and shellfish, a confirmatory method is needed as only one ion was validated. The missing data on the second fragment ion for the fish and shellfish HPLS/MS/MS study is to be provided at the latest 6 months prior to date of approval to the original Rapporteur Member State (Norway). If a second ion cannot be identified due to the small size of the molecule, confirmation can be addressed by a different approach. However, new information submitted recently, which is not fully evaluated, indicate that the residues in fish consist of metabolites which are rapidly excreted and not parent material. If this fact is confirmed, the data requirement for further analytical validation is redundant.

When re-assessing the approval of DCOIT in PT 21, the market share has to be verified.

In order to address a potentially severe underestimation of the risk to sediment dwelling organisms from exposure via suspended matter, caused by the fact that sorption data (Koc) has only been studied at concentrations which are not fully relevant in the marine environment, a new study on sorption at environmentally relevant conditions (concentrations µg/l to ng/l, pH ~8, DOC not too high, etc.) is to be performed before the antifouling active substances are evaluated for a potential renewal of the approval.

3.5 UPDATE OF THIS EVALUATION REPORT

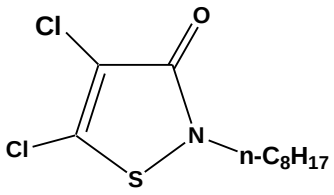
This evaluation report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the submitted information in relation with Regulation (EU) No 528/2012. Such adaptations will be examined and finalized in connection with any amendment of the conditions for the approval of DCOIT.

APPENDIX I: LIST OF ENDPOINTS

Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling

Active substance (ISO Common Name)	No ISO name accepted or proposed.
Function (*e.g.* fungicide)	Broad spectrum antifouling biocide
Rapporteur Member State	Norway

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	4,5-Dichloro-2-octylisothiazol-3(*2H*)-one
Chemical name (CA)	4,5-Dichloro-2-octyl-3(2H)isothiazolone
CAS No	64359-81-5
EC No	264-843-8
Other substance No.	ENCS No. 5-6165; ECL Serial No. 93-6 (MOL)
Minimum purity of the active substance as manufactured (g/kg or g/l)	950 - 1000 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	The active substance as manufactured does neither contain additives nor relevant impurities.
Molecular formula	$C_{11}H_{17}Cl_2NOS$
Molecular mass	282.2 (g/mol)
Structural formula	

Physical and chemical properties (Annex IIA, point III, unless otherwise indicated)

Melting point (state purity)	41.1-41.7°C (purity >98%)
Boiling point (state purity)	Boiling point is not applicable as decomposition occurs
Temperature of decomposition	297.9°C
Appearance (state purity)	Off-white solid at 20°C (purity >99%)
Relative density (state purity)	1.27 g/cm^3 at 25°C (purity >98%)
Surface tension	70.8 mN/m at 19°C
Vapour pressure (in Pa, state temperature)	9.8 x 10^{-4} Pa at 25°C 2.2 x 10^{-3} Pa at 30°C 4.6 x 10^{-3} Pa at 35°C
Henry's law constant (Pa m^3 mol $^{-1}$)	3.30 x 10^{-2} Pa m^3 mol^{-1} at 20°C and pH 7
Solubility in water (g/l or mg/l, state temperature)	pH__5____:2.85 mg/l at 10°C 4.26 mg/l at 20°C 6.68 mg/l at 30°C
	pH__7____:2.26 mg/l at 10°C 3.47 mg/l at 20°C 5.67 mg/l at 30°C
	pH__9____: Technically not possible (hydrolysis)
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	At 30°C: Solubility in both hexane and ethyl acetate is >1000 g/L At 10° C: Solubility in Hexane is 133.6 g/L; Solubility in Ethyl acetate is 322.9 g/L
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	Storage of pre-formulation (o-xylene) for 24 months at 20 and 30 °C. A.s. stable in o-xylene.
Partition coefficient (log K_{OW}) (state temperature)	pH___7___ and 23°C: 2.8
	This value will not vary as a function of pH and/or temperature.
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	Not applicable, DCOIT does not dissociate.

UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Neutral pH: λ_{max} at 284 nm ($\in$10314), 230 nm ($\in$5924); Acid pH: λ_{max} at 284 nm ($\in$10618), 230 nm ($\in$6100); Basic pH λ_{max} at 227 nm ($\in$13527)
Quantum yield of direct phototransformation in water at Σ > 290 nm (point VII.7.6.2.2)	Not determined.
Flammability	Not highly flammable Not auto-flammable Auto-Ignition Temperature: 264°C
Explosive properties	Not explosive/Not applicable.

Classification and proposed labelling (Annex IIA, point IX.)

with regard to physical/chemical data	-
with regard to toxicological data	Symbol: T+ (Very toxic), C (Corrosive) (optional: Xn, Xi) R-phrases : 21/22: Harmful in contact with skin and if swallowed 26: Very toxic by inhalation 34: Causes burns 37: Irritating to respiratory system 43: May cause sensitization by skin contact S-phrases : 22: Do not breathe dust 26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice 28: After contact with skin, wash immediately with plenty of… (to be specified by manufacturer) 36/37/39: Wear suitable protective clothing, gloves and eye/face protection 45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)
with regard to fate and behaviour data	S-phrase : 57: Use appropriate containment to avoid environmental contamination 60: This material and its container must be disposed of as hazardous waste
with regard to ecotoxicological data	Symbol: N (Dangerous for the environment) R-phrase: 50 : Very toxic to aquatic organisms 53: May cause long-term adverse effects in the aquatic environment *
Specific concentration limits	Setting specific lower concentration limits for sensitisation is warranted. A specific concentration limit of 0.001% is proposed. Setting specific concentration limit for corrosion/irritation should be considered DCOIT's high aquatic toxicity warrants specific concentration limits for the environmental effects. An M factor of 100 will be applied, due to the 24 hours E_rC_{50} of 1.6 µg/L from the *N. pelliculosa* study.

* See discussion on classification and labeling in Document I, chapter 2.1.4

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	High Performance Liquid Chromatography with UV detector (254 nm).
Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	High Performance Liquid Chromatography with UV detection (210 nm)

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	Extraction followed by LC/MS; LOQ= 0.05 µg/g.
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Trap airborne DCOIT on silica gel, extract and analyze by HPLC/MS/MS; LOQ=0.2 µg/m^3.
Water (principle of method and LOQ) (Annex IIA, point 4.2)	Liquid/liquid extraction followed by Capillary GC with Electron capture detector (ECD); LOQ=0.02 µg/L. Confirmation of the specificity of the method by Nitrogen Phosphorous Detector (GC-NPD).
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	Not required from a scientific point of view.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not required.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Fish and shellfish: Extraction and clean-up of the samples followed by HPLC/MS/MS; LOQ=0.01 mg/kg.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals (Annex IIA, point 6.2)

Rate and extent of oral absorption:	Close to 20% of DCOIT was excreted in the urine following oral administration. As the contribution of biliary excretion to the elimination of DCOIT is not known the amount of DCOIT in the faeces that has actually been absorbed is uncertain. As the main metabolites in the faeces may have been formed by biodegradation in the GI tract they do not give additional information about the oral absorption of DCOIT. In conclusion, the oral absorption is assumed to be moderate, and the value 20 is taken forward to the risk characterization.
Rate and extent of dermal absorption:	A high penetration of DCOIT dissolved in acetone or DPGME into the skin of rats has been shown and dermal delivery factors between 17% and 70% are estimated, dependent of exposure duration. The absorption rate is relatively low and 24% or less of the administered dose was systemically available in a 3 day period following DCOIT administration. Hair follicles seem to be major portal of entry for DCOIT. Dermal delivery values of 51% for DCOIT in concentrations of approximately 0.25% and 31% for DCOIT concentrations above 2% as well as systemic available doses of 24% for DCOIT in concentrations of approximately 0.25% and 22% for DCOIT concentrations above 2% have been established. The results obtained from two in vitro studies in human skin on antifouling paint formulations suggest that the absorption of DCOIT in an antifouling paint formulation through human epidermis is low when compared with the absorption of DCOIT diluted in solvent (without polymer). Based on these studies a dermal absorption value of 6% was derived.
Distribution:	Oral: excreta. Dermal: skin, excreta, carcass.
Potential for accumulation:	No evidence of accumulation in the animal body.
Rate and extent of excretion:	Rapidly eliminated following oral administration, primarily in faeces; oral: 62-95% of ^{14}C label by day 4; dermal: 1-20% of ^{14}C label by 24 h.
Toxicologically significant metabolite	Extensively metabolised. None of the metabolites are considered to be of concern.

Acute toxicity (Annex IIA, point 6.1)

LD_{50} oral	1636 mg/kg bw (rat); 567 mg/kg bw (mouse)
LD_{50} dermal	Tested in a concentrated biocidal pre-formulation (32.6 % DCOIT in xylene) > 652 mg ai/kg bw (rabbit)
LC_{50} inhalation	0.26 mg ai/L air (rat)

Skin irritation	Corrosive (rabbit). 0.5 ml of 32.6% solution of DCOIT in xylene applied undiluted (concentrated pre-formulation).
Eye irritation	Regarded as corrosive due to effects on skin.
Skin sensitization (test method used and result)	Maximization test (Magnusson-Kligman) = sensitizer at 0.01% (guinea pig).

Repeated dose toxicity (Annex IIA, point 6.3)

Species/ target / critical effect	Dog, rat/Irritation at site of administration.
Lowest relevant oral NOAEL / LOAEL	(i) Dog (90d): NOAEL = 300 ppm diet in dogs (10.2 mg/kg/day in males; 10.1 mg/kg/day in females) based on minimal changes in body weight, feed consumption, haematology and clinical chemistry parameters. (ii) Rat (28d): NOAEL = 20 mg/kg bw/day Changes in clinical chemistry, and haematology parameters were observed at 100 and 500 mg/kg bw. The changes indicate liver toxicity, but histology revealed no liver changes. Histopathology revealed local effects on the gastrointestinal tract at 100 and 500 mg/kg bw: Effects on spleen and adrenal cortex observed.
Lowest relevant dermal NOAEL / LOAEL	Tested with concentrated biocide pre-formulation (35% DCOIT in mixed xylenes) in rabbits (21d). LOAEL = 0.35 mg a.i/kg bw/day for local effects NOAEL = 1.75 mg a.i./kg bw/day for systemic effects, highest dose tested. Skin irritation was observed, but no apparent systemic toxicity.
Lowest relevant inhalation NOAEL / LOAEL	Tested with concentrated biocide pre-formulation (32.6% DCOIT in o-xylene) in rat (13 weeks). NOAEC = 0.02 mg a.i./m^3 (rat) LOAEC = 0.63 mg a.i./m^3 , based on respiratory tract irritation. No systemic toxicity was seen at any dose.

Genotoxicity (Annex IIA, point 6.6)	Not mutagenic

Carcinogenicity (Annex IIA, point 6.4)

Species/type of tumour	Not tested, but considered not carcinogenic
lowest dose with tumours	Not tested, but considered not carcinogenic

Reproductive toxicity (Annex IIA, point 6.8)

Species/ Reproduction target / critical effect	No effects on reproductive performance, hormone disruption or teratogenicity in rats
Lowest relevant reproductive NOAEL / LOAEL	Parental: NOAEL = 400 ppm (30-39 mg/kg bw/day in males)

	NOAEL = 400 ppm (33-41 mg/kg bw/day in females) Highest dose tested: 235 and 259 mg ai/kg bw/day, males and females, respectively Offspring: NOAEL = 200 ppm (16-21 mg/kg bw/day)
Species/Developmental target / critical effect	No adverse developmental effects in rats or rabbits (not teratogenic)
Lowest relevant developmental NOAEL / LOAEL	NOAEL = 10 mg/kg bw/day (maternal rat); NOAEL = 30 mg/kg bw/day (fetal rat); Highest dose tested: 100 mg/kg bw/day (rat); 300 mg/kg bw group terminated due to severe maternal toxicity.

Neurotoxicity / Delayed neurotoxicity (Annex IIIA, point VI.1)

Species/ target/critical effect	No evidence of neurotoxicity in other multiple dose studies.
Lowest relevant developmental NOAEL / LOAEL.	No evidence of neurotoxicity in other multiple dose studies.

Other toxicological studies (Annex IIIA, VI/XI)

DCOIT Technical was neither irritating nor sensitizing to the skin of humans in petrolatum or corn oil at concentrations up to and including 1000 ppm a.i. Studies of DCOIT Technical in ethanol demonstrated that 250-350 ppm a.i. is at or near the threshold concentration for irritation and sensitization in humans.

Medical data (Annex IIA, point 6.9)

Not available

Summary (Annex IIA, point 6.10)	Value	Study	Safety factor
ADI (if residues in food or feed)[1]	0.1 mg/kg	90-day dietary study (dog)	100
AEL acute[2]	0.04 mg/kg	28-day gavage study (rat)	100
AEL medium term[2]	0.02 mg/kg/day	90-day dietary study (dog)	100
AEL long term[3]	0.02 mg/kg/day	90-day dietary study (dog)	100
AEC dermal[4]	0.7 µg/cm^2, 0.003% (w/v)	Repeated exposure human patch tests (DCOIT in ethanol)	9.6 (LOAEC to NOAEC extrapolation 3, interspecies factor 1, intraspecies 3.2)
AEC inhalation (long term)[4]	0.013 mg/ m^3 (≈ 0.01mg/m^3)	13 week nose-only study (rat).	48 (LOAEC to modified NOAEC extrapolation 3, interspecies 2.5, intraspecies 3.2, subchronic to chronic

AEC inhalation (medium term)[4]	0.026 mg/m^3 (≈ 0,03 mg/m^3)		exposure 2) 24 (LOAEC to NOAEC extrapolation 3, interspecies 2.5, intraspecies 3.2)
Drinking water limit	0.1 µg/L	Directive 98/83/EC [5]	N/A
ARfD (acute reference dose)[1]	0.2 mg/kg	28-day gavage study (rat)	100
	The primary human health hazards associated with DCOIT are irritation of the skin, eyes, intestinal tract or lungs, as well as, allergy following repeated skin contact. There is no evidence of significant systemic toxicity at doses below those that gives significant local irritation.		

[1] External reference values, no correction for oral absorption
[2] Corrected for oral absorption (20 %)
[3]There is no chronic study upon which a long term AEL can be based, due to a well documented waving proposal. However, as local irritation is dominating and potential adverse systemic effects seems to occur at higher doses, the Rapporteur proposes that the AEL long term is set at the same level as the AEL medium term (0.02 mg/kg bw/day).
[4]The relevance of these AEC values for products is questionable as the formulation will have significant impact on the potential for local effects of the substance
[5] As for any pesticide

Acceptable exposure scenarios (including method of calculation)

Production of a.s/ preformulation and paint formulation	Production of active substance/pre-formulation takes currently place outside the EU; hence, description of the manufacturing process for exposure purposes is not needed. Exposure of plant workers during the formulation of biocidal products is not within the scope of Biocidal Products Directive and has not been addressed as other legislation applies.
Professional users	Ready for use products applied by trained professionals only - by high pressure airless spraying or brush and roller (spot applications, smaller objects). Scenarios assessed: spray painter (ships hulls), painter using roller and brush (spot application), painter using spray equipment or roller and brush (other structures), pot-man, ancillary workers, paint stripper and grit filler. Two representative formulations assessed; • A theoretical product with 3% DCOIT • A real product with 2 % DCOIT Exposure assessment based generic exposure data: Simple database models in TNsG of Human exposure to biocidal products of 2002 as updated in the User Guidance and raw data behind these models. Exposure data published after the first TNsG on human exposure/User Guidance considered as well. Results from two worker exposure studies conducted by Rohm and Haas Company included for information. Dermal absorption: 6%. (Tier 1 for theoretical product: 100%) PPE: protective gloves and footwear, protective clothing (single or double layer of coverall. Assigned protection factor 20 or 100.) When available, actual measurements inside gloves/protective clothing were used in the exposure calculations. RPE: Assigned protection factor of 10 or 40 Risk assessment and proposed RRM for theoretical product based on an evaluation of local effects as well as systemic effects. Exposure above the threshold values for systemic effects and respiratory irritation for most scenarios, assuming use of appropriate PPE/RPE. In use concentration far above the external reference values for local dermal effects. However, the relevance of these

	external reference values for the products is questionable as the formulation will have significant impact on the potential for local effects of the substance. The composition of an antifouling paint formulation seems to reduce both the potential for irritation and the dermal penetration of the substance. Hence, for the real product a risk assessment was based on an evaluation of systemic effects in addition to an assessment of local respiratory effects. An acceptable exposure level was calculated for all scenarios except the one for potman (borderline risk identified for ancillary workers) when based on the more superior/relevant exposure data, assuming use of appropriate PPE/RPE. The risk of local effects on skin, eyes and respiratory tract (sensitization and/or irritation) as well as potential systemic effects from DCOIT must be controlled through the use of suitable risk management measures, including process optimisation, engineering control and appropriate and suitable PPE/RPE. A system of health surveillance (regular skin inspection and recording, by a trained individual) should be in place. For result of the exposure calculations: See Table 2.5 and Table 2.6 to Assessment Report.
Non-professional users	Not relevant. Evaluated only for us by professionals.
Indirect exposure as a result of use	Indirect exposure via the environment (seafood): Risk to consumers from consumption of fish and other seafood contaminated by DCOIT not expected based on a simplified risk assessment..

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH__4____: 260 days at 25°C; 93 days at 40°C (normalized to 12°C: 736 and 874 days)
	pH__7____: 71 days at 25 °C; 19 days at 40°C (normalized to 12°C: 201 and 178 days)
	pH__8____: 148 days at 9 °C (marine conditions) (extrapolated from the measurements at pH 4, 7 and 9)
	pH___9___: 3.5 days at 25°C; 0.6 days at 40°C (normalized to 12°C: 10 and 5.6 days)
	No metabolites formed in amounts > 10 % at environmentally relevant pH and temperature.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	DT_{50}=13.4 days (light); 79.7 days (dark) at 25°C, pH 7 (normalized to 12°C – freshwater: 38 and 225 days) (normalized to 9°C – seawater: 48 and 287 days)
	31 % N-(n-octyl) oxamic acid. No data on photolysis of the relevant metabolite available
Readily biodegradable (yes/no)	No However, DCOIT inhibited the microorganisms in the ready biodegradation test
Readily biodegradable, metabolites (yes/no)	N-(n-octyl) malonamic acid (NNOMA): Yes N-(n-otyl) acetamide (NNOA): Yes 2-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid: No
Biodegradation in estuarine water	DT_{50} = 8.6-34.6 hours at 9°C DT_{50} = 6.8-27.8 hours at 12°C Metabolites: • N-(n-octyl) oxamic acid NNOOA (24%) • 2-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid (max. 12%) • 1-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid (max. 9%) No CO_2 development monitored
Non-extractable residues	40-65% of the applied ^{14}C-activity in the water-sediment studies after 100 days in the freshwater studies, 30 days in the aerobic seawater-sediment study and 365 days in the anaerobic seawater-sediment study. This activity exists as metabolites since it has been shown that parent can be readily extracted and quantified. A large portion is not extractable and associated with the humin, probably due to the octyl chain intercalating within the sediment crystal lattice.

Distribution in water / sediment systems (active substance)	DCOIT is rapidly eliminated from water-sediment systems. The dissipation half-lives are: **Freshwater** Aerobic study: DT_{50} = 1.6 days (12°C) Anaerobic study: DT_{50} = 0.17 days (12°C) **Seawater:** Aerobic study: DT_{50} < 3.6 hours (9°C) Anaerobic study: DT_{50} < 3.6 hours (9°C) DCOIT could almost not be detected in sediment. ^{14}C in sediment comprises of metabolites since it has been shown that parent can be readily extracted from sediment and quantified. CO_2 development in the water-sediment studies was between 5 and 20 % of applied radioactivity. 40-65% NER; DCOIT and its metabolites become rapidly and tightly associated with the sediment surface.
Distribution in water / sediment systems (metabolites)	In the freshwater-sediment studies none of the metabolites were > 10%. In the aerobic seawater-sediment study the major metabolites were: • N-(n-octyl) malonamic acid NNOMA (16%) • N-(n-octyl) acetamide NNOA (12.4%) No metabolic profile is available for the anaerobic seawater-sediment study. The metabolites become rapidly and tightly associated with the sediment surface.

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

Mineralization (aerobic)	CO_2 was present at 11-21% of the applied activity after 32 days of incubation
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (12°C, aerobic): 4.7 days (geometric mean; single first order DT_{50}). R^2 = 0.95 Two different soil types (silt loam and loamy sand) have been tested at two different temperatures (6 and 25°C).
	DT_{90lab} (20°C, aerobic): not available
	DT_{50lab} (20°C, anaerobic): not available
	Degradation in the saturated zone: not applicable
Field studies (state location, range or median with number of measurements)	DT_{50f}: not available
	DT_{90f}: not available
Anaerobic degradation	Not available
Soil photolysis	Not available
Non-extractable residues	41-54 % of the applied ^{14}C-activity becomes incorporated into the bound residues (none of which is parent). Acid hydrolysis extracted only a small portion of the bound residues (15%). NaOH extraction released about 65% of the bound residues of which a significant portion was associated with the humic acid fraction.

	Approximately 20% of the post extraction solids was not extractable with base and was retained in the inorganic humin fraction.
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	CO_2 was the major metabolite being present at 11-21% of the applied activity. This demonstrates cleavage of the isothiazolone ring and that significant metabolism of the resulting alkyl metabolites has occurred. Sixteen additional non-CO_2 metabolites were detected by HPLC; however, no definitive metabolite identification analysis was performed. However, the metabolic pathway and profile is expected to be similar to the findings in aquatic environment. Only one metabolite and at only one sampling interval was present at greater than 10% (ca. 11%) of the applied dose.
Soil accumulation and plateau concentration	No accumulation of DCOIT in soil as a result of quick biodegradation.

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

Ka , Kd Ka_{oc} , Kd_{oc}	K_a in soil = 41-214; K_a in sediment = 698-1147 K_d in soil = 101-798; K_d in sediment = 1413-2401 Ka_{oc} in soil = 5659-25237; **mean value 12169** Ka_{oc} in sediment = 17232-**28320** Kd_{oc} in soil = 18052-64250 Kd_{oc} in sediment = 34887-59282 Unit for all values is mg/L
pH dependence (yes / no) (if yes type of dependence)	Not expected

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

Direct photolysis in air	The phototransformation rate constants and half-lives were calculated using structure activity relationship (SAR) methods. The rate constant, k, was calculated from the OH and NO_3 radical reaction processes and the resulting rate constant used to calculate the half-life. The calculated half-lives for both OH and NO_3 radical reactions were 12.4 and 27.5 hours, respectively. For the observed metabolites and degradation products of DCOIT the half-lives range from 18.6 to 24.4 hours.
Quantum yield of direct photolysis	Not available
Photo-oxidative degradation in air	Latitude:- N/A..... Season:- N/A..... DT_{50}: N/A.....
Volatilization	Insignificant due to low vapour pressure and Henry's law constant.

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	Not available
Surface water and sediment (indicate location and type of study)	See overview in chapter 2.2.2.7 of Doc I / the Assessment Report
Ground water (indicate location and type of study)	Not available
Air (indicate location and type of study)	Not available

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	Endpoint	Toxicity
Freshwater Fish			
Rainbow trout (*Salmo gairdneri*)	Acute-96 hr, flow-through	LC_{50} LC_0	2.7 µg a.i./L (mm)* 1.8 µg a.i./L (mm)
Rainbow trout (*Salmo gairdneri*)	Chronic 97 days early life stage toxicity flow-through	NOEC, egg hatch, survival LOEC, egg hatch, survival NOEC, growth LOEC, growth	1.2 µg a.i./L (mm) 2.6 µg a.i./L (mm) 0.56 µg a.i./L (mm) 1.2 µg a.i./L (mm)
Saltwater Fish			
Japanese Blowfish (*Takifugu rubripes*)	Acute-96 hr semi-static	LC_{50} LC_0	5.66 µg a.i./L (n)* 3.67 µg a.i./L (n)
Sheepshead minnow (*Cyprinodon variegatus*)	Chronic 35 days early life stage toxicity flow-through	NOEC, egg hatch, survival LOEC, egg hatch, survival MATC, egg hatch, survival	6.0 µg a.i./L (mm) 14 µg a.i./L (mm) 9.2 µg a.i./L (mm)
Freshwater Invertebrates			
Daphnia magna	Acute-48 hr flow-through	EC_{50} EC_0	5.2 µg a.i./L (mm) 3.9 µg a.i./L (mm)
Daphnia magna	Chronic-21 days flow-through	NOEC, survival of first generation LOEC, survival of first generation MATC, survival of first generation	0.63 µg a.i./L (mm) 1.1 µg a.i./L (mm) 0.83 µg a.i./L (mm)

* mm = mean measured concentrations; n = nominal concentrations

Species	Time-scale	Endpoint	Toxicity
Saltwater Invertebrates			
Mysid (*Mysidopsis bahia*)	Acute-96 hr flow-through	LC_{50} LC_0	4.7 µg a.i./L (mm)* 1.6 µg a.i./L(mm)
American oyster embryo (*Crassostrea virginica*)	Acute-48 hours, static in synthetic and natural seawater	Synt.: EC_{50} NOEC EC_{10} Natural: EC_{50} NOEC EC_{10}	12 µg a.i./L (n); 2.1 µg a.i./L (mm) 10 µg a.i./L (n) 0.2 µg a.i./L (mm) 24 µg a.i./L (n); 3.2 µg a.i./L (mm) 18 µg a.i./L (n) 0.5 µg a.i./L (mm)
Bay mussel embryo (*Mytilus edulis*)	Acute-48 hours, static	EC_{50} NOEC	411 µg a.i./L (mm) 207 µg a.i./L (mm)
Mysid (*Americamysis bahia*)	Chronic-28 days flow-through	NOEC, survival of first generation LOEC, survival of first generation MATC, survival of first generation	0.63 µg a.i./L (mm) 1.24 µg a.i./L (mm) 0.882 µg a.i./L (mm)
Freshwater Algae			
Navicula pelliculosa	96 hours EC_{50} and NOEC	24 h E_rC_{50} 24 h NOE_rC	1.6 µg a.i./L (m)* 0.34 µg a.i./L (m)
Saltwater Algae			
Skeletonema costatum	120 hr EC_{50} and NOEC	24 h E_rC_{50} 24 h NOE_rC	0.48µg a.i./L (m) 0.48 µg a.i./L (m)
Freshwater sediment dwelling organisms			
Midge larvae (*Chironomus tentans*)	Acute-10 days flow-through	NOEC LC_{50}	6.3 mg ^{14}C equiv/kg dwt (n) 19.9 mg ^{14}C equiv/kg dwt (n)
Midge larvae (*Chironomus riparius*)	Chronic-28 days, artificial sediment static	10 d-NOEC, survival 10 d-LOEC survival	3.09 mg a.i./kg dwt (mm) 4.9 mg ^{14}C equiv/kg dwt (mm) 6.59 mg a.i./kg dwt (mm) 9.7 mg ^{14}C equiv/kg dwt (mm)

* mm = mean measured concentrations; n = nominal concentrations ; m = initial measured concentrations

Species	Time-scale	Endpoint	Toxicity
Saltwater sediment dwelling organisms			
Amphipods (*Leptocheirus plumulosus*)	Chronic-28 days, natural sediment static	NOEC, survival LOEC, survival	0.1 mg a.i./kg dwt* 10 mg ^{14}C equiv/kg dwt (mm) 0.17 mg a.i./kg dwt (mm) 19 mg ^{14}C equiv/kg dwt (mm)
Microorganisms			
Activated sludge respiration inhibition	Acute-3 hr	EC_{50} EC_{15}	>5.7 mg a.i./L 0.64 mg a.i./L
Aquatic Plants			
Duckweed *(Lemna gibba)*	Acute-7 days static	EC_{50}, growth rate 3 days NOEC, normal frond number, 3 days NOEC, area under the growth curve, growth rate	206 µg a.i./L (m) 4.50 µg a.i./L (m) 4.54 µg a.i./L (m)

* estimated value

mm = mean measured concentrations; m = initial measured concentrations

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

Species	Time-scale	Endpoint	Toxicity
Freshwater Fish-NNOMA			
Rainbow trout (*Salmo gairdneri*)	Acute-96 hr	LC_{50} LC_0	250 mg a.i./L 160 mg a.i./L
Freshwater Fish-NNOA			
Rainbow trout (*Salmo gairdneri*)	Acute-96 hr	LC_{50} LC_0	25 mg a.i./L 11 mg a.i./L
Freshwater Invertebrates-NNOMA			
Daphnia magna	Acute-48 hr	EC_{50} EC_0	157 mg a.i./L 69 mg a.i./L
Freshwater Invertebrates-NNOA			
Daphnia magna	Acute-48 hr	EC_{50} EC_0	28 mg a.i./L 9.5 mg a.i./L
Freshwater Algae-NNOMA			
Selenastrum Capricornutum	96 hr EC_{50}	E_rC_{50} NOE_rC	9.70 mg a.i./L 1.51 mg a.i./L
Freshwater Algae-NNOA			
Selenastrum Capricornutum	96 hr EC_{50}	72 h E_rC_{50} 72 h NOE_rC	11 mg a.i./L (initial measured concentrations) 2.7 and 1.99 mg a.i./L based on initial and mean measured concentrations, respectively
Saltwater Algae-NNOMA			
Skeletonema costatum	96 hr EC_{50}	E_rC_{50} NOE_rC	0.47 mg a.i./L 0.13 mg a.i./L

Effects on earthworms or other soil non-target organisms

Acute toxicity to Earthworm (*Eisenia foetida*) (Annex IIIA, point XIII.3.2)	LC_{50} = 250 mg a.i./kg soil NOEC (14-d survival, sub-lethal behaviour) = 130 mg a.i./kg wwt NOEC (14-d weight change) = 500 mg a.i./kg wwt
Reproductive toxicity to Earthworm (*Eisenia foetida)* (Annex IIIA, point XIII.3.2)	NOEC (28-d survival and growth) = 160 mg a.i./kg dwt NOEC (56-d reproduction) = 5 mg a.i./kg dwt (initial) NOEC (56-d reproduction) = 3.5 mg a.i./kg dwt (TWA) LC_{50} (28-d survival and growth) >160 mg a.i./kg dwt LC_{50} (56-d reproduction) = 25.9 mg a.i./kg dwt

Effects on soil micro-organisms (Annex IIA, point 7.4)

Nitrogen mineralization	EC_{50} = 155 mg a.i./kg dwt EC_{10} = 42.9mg a.i./kg dwt
Carbon mineralization	EC_{50} = 393 mg a.i./kg dwt EC_{10} = 15.3 mg a.i./kg dwt

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	See chapter 3 of LOE
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	Mallard duck: LD_{50} > 3,580 mg a.i./kg bw (single dose) LD_0 > 3,580 mg a.i./kg bw NOAEL > 1,660 mg a.i./kg bw
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	Bobwhite quail: LC_{50} > 4,640 mg a.i./kg food (5 days feeding) LC_0 = 2,500 mg a.i./kg food NOEC = 1,250 mg a.i kg food (mortality; 5 days feeding) Mallard duck: LC_{50} > 4,640 mg a.i./kg food (5 days feeding) LC_0 = 625 mg a.i./kg food NOEC = 625 mg a.i.kg food (mortality; 5 days feeding)
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	Not available

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not available
Acute contact toxicity	Not available

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not available
Acute contact toxicity	Not available
Acute toxicity to ……..	Not available

Bioconcentration (Annex IIA, point 7.5)

Bioconcentration factor (BCF)	Bluegill sunfish : Steady state BCF = 750 ($K_{uptake}/K_{depuration}$, total ^{14}C-residues) Total ^{14}C-residue BCF: • Fillets: 7-200 L/kg • Viscera: 110-1300 L/kg • Whole fish: 56-660 L/kg Active substance BCF < 13 L/kg Oyster : Kinetic BCF ($K_{uptake}/K_{depuration}$) = 19-44 (total ^{14}C-residues)
Depuration time(DT_{50}) (DT_{90})	Bluegill sunfish : DT_{50} = 11.6 days Oyster : DT_{50} = 16-42 days
Level of metabolites (%) in organisms accounting for > 10 % of residues	Residues were ring cleaved compounds associated with proteins (a cysteine conjugate was identified). However, metabolites have not been identified and/or quantified. Very little if any DCOIT was detected in fish.

Chapter 6: Other End Points

Effects on Terrestrial plants (Document IIIA, point 7.5)

Terrestrial Plants			
Canola, Red Clover, and Rice	Seedling emergence and seedling growth-21 days Soil incorporation	Canola[1] :	
		NOEC Shoot length	5.0 mg a.i./kg dwt
		EC_{50} Shoot length	19 mg a.i./kg dwt
		Red Clover[1] :	
		NOEC Shoot dry weight	5.0 mg a.i./kg dwt
		EC_{50} Shoot dry weight	13 mg a.i./kg dwt
		Rice[1] :	
		NOEC Shoot lenght	6.1 mg a.i./kg dwt
		EC_{50} Shoot lenght	23 mg a.i./kg dwt
		NOEC Shoot dry weight	10 mg a.i./kg dwt
		EC_{50} Shoot dry weight	16 mg a.i./kg dwt
Canola, Red Clover, and Rice	Vegetative vigor Foliar spray	Canola[1] :	
		NOEC Shoot dry weight	2.6 mg a.i./kg dwt
		EC_{50} Shoot dry weight	8.6 mg a.i./kg dwt
		Red Clover[1] :	
		NOEC Shoot dry weight	0.12 mg a.i./kg dwt
		EC_{50} Shoot dry weight	3.1 mg a.i./kg dwt
		Rice[1] :	
		NOEC Shoot dry weight	0.64 mg a.i./kg dwt
		EC_{50} Shoot dry weight	> 41 mg a.i./kg dwt

[1] : most sensitive parameter

APPENDIX II: LIST OF INTENDED USES

Summary of intended uses[7]

DCOIT has been evaluated for its intended use as an antifouling a.s. on parts of ships, boat hulls and static structures. There will be no application to boats under 25 m in overall length, so only large marine-going vessels and super yachts will be treated.
The product is intended for use by professional operators only.

Object and/or situation	Member State or Country	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment			Remarks
				Type	Conc. of as	method kind	number min max	interval between applications (min)	g as/L min max	water L/m^2 min max	g as/m^2 min max	
Ship hulls commercial boats and superyachts (>25 m)	EU	DCOIT containing antifouling products	Fouling organisms (bacteria, fungi, algae, barnacles, ...)	Anti-fouling paint	1-3 %	Airless spray Brush/ roller	1-3 coats	Service life : 18-60 months	20-60 g/L	Paint coverage 5 m^2/L (typical)	4-12 g/m^2	
Buoys												
Other structures (sluice doors, off-shore structures) submerged in marine and brackish/estuarine water												

[7] adapted from: EU (1998a): European Commission: Guidelines and criteria for the preparation of complete dossiers and of summary dossiers for the inclusion of active substances in Annex I of Directive 91/414/EC (Article 5.3 and 8,2). Document 1663/VI/94 Rev 8, 22 April 1998

APPENDIX III – LIST OF STUDIES

List of studies for the active substance

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
III-A3/01	Broughton, H.S.	1994	Product Chemistry Kathon® 287T Biocide Technical grade of Active Ingredient. Rohm and Haas Company, Report N° TR-94-25, GLP, Unpublished.	Y(ii)[8]	N	Rohm and Haas
III-A3/02	Petigara, R.B.	2001	Biocides Product Directives Common Core Data Set for Active (Chemical) Substances, Parts 2 and 3: Identity, and Physical and Chemical Properties of Kathon® 287T Biocide. Rohm and Haas Company, Report N° TR-01-061, GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A3/03	Cihiy, J.S.	1996	Product Chemistry Series 63 : Physical and Chemical Characterization Studies of Kathon® 287T Biocide. Rohm and Haas Company, Report N° TR-96-08, GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A4.1.a/01	Doshi D.R.	2004a	Reverse phase HPLC analysis for 4,5-dichloro-n-octyl-4-isothiazolin-3-one or DCOIT (RH-287) in Technical. Rohm and Haas Company, Report N° CIS-TM-91-22-05, Unpublished.	Y(ii)	N	Rohm and Haas
III-A4.1.a/02	Doshi D.R.	2003	Reverse phase HPLC analysis for 4,5-dichloro-n-octyl-4-isothiazolin-3-one or DCOI (RH-287) in Technical. Rohm and Haas Company, Report N° CIS-TM-91-22-04, Unpublished.	Y(ii)	N	Rohm and Haas
III-A4.1.a/03	Doshi D.R.	2001	Reverse phase HPLC analysis for 4,5-dichloro-n-octyl-4-isothiazolin-3-one (RH-287) in Technical and formulations. Rohm and Haas Company, Report N° CIS-TM-91-22-03, Unpublished.	Y(ii)	N	Rohm and Haas
III-A4.1.a/04	Doshi D.R.	2002	Validation of CIS analytical method 91-22-03 Draft HPLC method to determine active ingredient (AI) in 4,5-dichloro-n-octyl-4-isothiazolin-3-one (RH-287) in technical and formulations. Rohm and Haas Company, Report N° TR-01-030, GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A4.1.a/05	Doshi D.R.	2004b	Validation of CIS analytical method 91-22-04 HPLC analysis to determine active ingredient (AI) in 4,5,-dichloro-n-octyl-4-isothiazolin-3-one (DCOIT or RH-287) in Technical Material. Rohm and Haas Company, Report N°	Y(ii)	N	Rohm and Haas

[8] Y(ii): Data protection claimed in accordance with Article 12.1(c) (ii): Active substance already on the market on 14 May 2000. Data submitted for the first time in support of the first inclusion in Annex I or IA or Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA (data generated after the entry into force of the Directive).

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
			GLP-2004-05, GLP, Unpublished.			
A4.1.b/01	Doshi, D.R.	2001	Validation of CIS Analytical method 01-74-01 Draft, HPLC method to determine impurities in 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one (RH-287) Technical. Rohm and Haas Company, Report N° TR-01-037, GLP, Unpublished. *This report contains confidential information.*	Y (ii)	N	Rohm and Haas
A4.1.b/02	Doshi, D.R.	2001	CIS Test Method # 01-74-01: Reverse phase HPLC analysis of RH-287 (4,5-dichloro-2-n-octyl-4-isothiazolin-3-one or DCOI) Technical for impurities. Rohm and Haas Company, Report N° CIS-TM-01-74-01, Unpublished. *This report contains confidential information.*	Y (ii)	N	Rohm and Haas
A4.1.c/01	Doshi, D.R.	2004	Validation of CIS Analytical method 04-90-01, a Capillary GC Method to determine impurity 4-bromo-5-chloro-2-n-octyl-4-isothiazolin-3-one (BCOIT) in 4,5-Dichloro-n-octyl-4-isothiazolin-3-one (RH-287 or DCOIT) Technical. Rohm and Haas Company Report N° TR-04-018, GLP, Unpublished. *This report contains confidential* information.	Y (ii)	N	Rohm and Haas
A4.1.c/02	Doshi, D.R.	2001	CIS Test Method # 04-90-02 : Capillary gas Chromatography Method to determine impurity BCOIT in RH-287 Technical. Rohm and Haas Company Report N° CIS-TM-04-90-02, Unpublished. *This report contains confidential information.*	Y (ii)	N	Rohm and Haas
A4.1.d/01	Berrios E.	2001	CIS Test Method # 01-76-01 : Capillary GC/FID analysis of RH-25287 Tech samples for residual solvents. Rohm and Haas Company, Report N° CIS-TM-01-76-01, Unpublished. *This report contains confidential information.*	Y (ii)	N	Rohm and Haas
A4.1.d/02	Berrios E.	2003	GLP validation of CIS analytical test method # 01-76-01. Rohm and Haas Company, Report N° GLP-2003-044, GLP, Unpublished. *This report contains confidential information.*	Y (ii)	N	Rohm and Haas
A4.1.e/01	Berrios E.	2005a	CIS Test Method # 05-101-02 : Reverse phase HPLC method of RH287 technical for monochlorobenzene Rohm and Haas Company, Report N° CIS-TM-05-101-02 (December 7, 2005), Unpublished. *This report contains confidential* information.	Y (ii)	N	Rohm and Haas
A4.1.e/02	Berrios E.	2005b	GLP validation of CIS analytical test method #05-101-02. Rohm and Haas	Y (ii)	N	Rohm and

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
			Company, Report N° GLP-2005-065 (December 7, 2005), GLP, Unpublished. *This report contains confidential information.*			Haas
III-A4.2.a	Marbo M.	2004	Validation of CIS Analytical Methods Numbered 03-83-01 and 04-87-91 to Determine Active Ingredient (AI) 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one (DCOIT or RH-287) in Soil and Sediment Samples. Rohm and Haas Company, Report N° TR-04-016, GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A4.2.b/01	Krainz, A.	2004	Test method for the determination of 4,5-dichloro-2-n-octyl-3(2H)- isothiazolone (DCOIT) in air. Source: RCC Ltd. Rohm and Haas Company. Study N° 846762, Unpublished.	Y(ii)	N	Rohm and Haas
III-A4.2.b/02	Krainz, A.	2003	Development and validation of a residue analytical method for DCOIT in air. Source: RCC Ltd. Rohm and Haas Company. Report N° GLP-2003-45, GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A4.2.c/01	Wais, A.	2003a	Test method to determine 2,4 Dichloro-n-octyl isothiazolone (DCOIT) in drinking, surface and sea water. Source: RCC Ltd. Rohm and Haas Company. Study N° 845577-03, Unpublished.	Y(ii)	N	Rohm and Haas
III-A4.2.c/02	Wais, A.	2003b	Validation of a residue analytical method for DCOIT in drinking, surface and sea water. Source: RCC Ltd. Rohm and Haas Company. Report N° GLP-2003-21, GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A4.3/01	Wolf, S.	2003a	Test method to determine 2,4 Dichloro-n-octyl isothiazolone (DCOIT) in fish and shellfish. Source: RCC Ltd. Rohm and Haas Company. Study N° 845576, Unpublished.	Y(ii)	Y	Rohm and Haas
III-A4.3/02	Wolf, S.	2003b	Validation of a residue analytical method for DCOIT in fish and shellfish. Source: RCC Ltd. Rohm and Haas Company. Report N° GLP-2003-058, GLP, Unpublished.	Y(ii)	Y	Rohm and Haas
III-A5.3.1/01	Williams T.M	2005	The Antimicrobial Activity of Dichloro-octylisothiazolinone (DCOIT): "Minimum Inhibitory Concentration (MIC) Studies versus Algae, Fungi, and Bacteria". Rohm and Haas Company, Report N° TR-05-009, Unpublished.	Y(ii)	N	Rohm and Haas
III-A6.1.1/01	xxx	1992	XB3 technical HQ (RH-287): acute oral	Y(i)[9]	N	Rohm

[9] Y(i) : Data protection claimed in accordance with Article 12.1(c) (i): Active substance already on the market on 14 May 2000. Information submitted for the purposes of the Directive. Information already submitted to the MS

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
	(confidential)		toxicity study in male and female rats. Rohm and Haas Company, Report N° 92R-066, GLP, Unpublished.			and Haas
III-A6.1.1/02	xxx (confidential)	1994	RH-287 technical: acute oral toxicity study in male and female mice, Rohm and Haas Company, Report N° 94R-003, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.1.2/01	xxx (confidential)	1989a	Antifoulant C-9211 HQ: acute dermal toxicity study in male and female rabbits; Rohm and Haas Company, Report N° 88R-225, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.1.3/01	xxx (confidential)	1994	RH-287 technical: acute inhalation toxicity study in rats; Rohm and Haas Company, Report N° 93R-217, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.1.3/02	xxx (confidential)	1992	Kathon™ 930 biocide: acute inhalation toxicity study in rats; Rohm and Haas Company, Report N° 91R-072, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.1.4/01	xxx (confidential)	1989b	Antifoulant C-9211 HQ: skin irritation study in rabbits; Rohm and Haas Company, Report N° 88R-226, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.1.5/01	xxx (confidential)	2003	RH-287 Technical: A dermal sensitization study in guinea pigs (Magnusson-Kligman method); Product Safety Labs Study Number 13215, Rohm and Haas Company Report N° 02RC-106, GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A6.1.5/02	xxx (confidential)	2006	N-(n-octyl) malonamic acid: Local lymph node assay; Calvert Report N° 0787MR07.015, Rohm and Haas Company, Report N° 05RC-044 (January 16, 2006), GLP, Unpublished	Y(ii)	N	Rohm and Haas
III-A.6.2.a/01	xxx (confidential)	1994	^{14}C-RH-287: pharmacokinetic study in rats; Rohm and Haas Company, Report N° 92R-073, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A.6.2.a/02	xxx (confidential)	1996	^{14}C-RH-5287: metabolism in rats; Rohm and Haas Company, Report N° TR34-96-153, GLP, Unpublished. (Supplemental study Rohm and Haas Report N° 92R-073).	Y(i)	N	Rohm and Haas
III-A6.2.b/01	xxx (confidential)	1994	^{14}C-RH-287: dermal absorption study in male rats; Rohm and Haas Company, Report N° 92R-074, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.3.1/01	xxx (confidential)	1991	Toxicity study of RH-287 by oral administration to SD rats for four weeks followed by a two-week recovery period; Mitsuibishi-Kasei Institute of Toxicological and Environmental Sciences Experiment N° 8K280-E, Rohm and Haas Company Report N° 89RC-1033, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.3.2/01	xxx	1983	C-9211M: 21-day dermal toxicity study in	Y(i)	N	Rohm

before 14 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA (data already submitted before the entry into force of the Directive).

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
	(confidential)		rabbits; Rohm and Haas Company, Report N° 82R-119, GLP, Unpublished.			and Haas
III-A6.4.1a/01	xxx (confidential)	1994	RH-287 Technical: three-month dietary toxicity study in rats; Rohm and Haas Company, Report N° 93R-249, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.4.1b/01	xxx (confidential)	2002	90-day dietary toxicity study of RH-287 technical in dogs; MPI Research Study N° 285-063, Mattawan, Michigan, USA, Rohm and Haas Company Report N° 01RC-086, GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A6.4.3/01	xxx (confidential)	1994	Antifoulant C-9211M HQ (RH-287): thirteen-week nose-only inhalation toxicity study in rats; Rohm and Haas Company, Report N° 89R-256, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.6.1/01	Sames J.L. and Elia M.C.	1994	RH-287 Technical: *Salmonella typhimurium* gene mutation assay (Ames test), Rohm and Haas Company, Report N° 93R-230, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.6.1/02	San, R.H.C. and Trombley, A.	2005	N-(n-octyl) malonamic acid: bacterial reverse mutation (Ames) assay, BioReliance AB13CF.503.BTL, Rohm and Haas Report N° 05RC-043 (September 7, 2005), GLP, Unpublished	Y(ii)	N	Rohm and Haas
III-A6.6.2/01	Kumaroo P.V.	1994	RH-287 technical: test for chemical induction of chromosome aberration in cultured Chinese hamster ovary (CHO) cells with and without metabolic activation, Sitek Research Laboratories Study N° 0258-3114, Rohm and Haas Report N° 93RC-233, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.6.3/01	Pant K.	1994	RH-287 Technical: Test for chemical induction of gene mutation at the HGPRT locus in cultured Chinese hamster ovary (CHO) cells with and without metabolic activation, Sitek Research Laboratories Study N° 0258-2500, Rohm and Haas Company Report N° 93RC-231, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.6.4/01	xxx (confidential)	2001	Kathon 287 technical: micronucleus assay in CD-1 mouse bone marrow cells, Rohm and Haas Company, Report N° 00R-077, GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A6.8.1a/01	xxx (confidential)	1986	A teratology study in rabbits with C-9211 formulation, WIL Research Laboratories Project N° WIL-91001, Rohm and Haas Report N° 85RC-59, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.8.1b/01	xxx (confidential)	1983	Teratology study of C-9211 M in the rat, Rohm and Haas Company, Report N° 82R-221, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.8.1b/02	xxx (confidential)	1994	RH-287 Technical: oral (gavage) developmental toxicity study in rats, Rohm and Haas Company, Report N° 93R-229, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.8.2/01	xxx (confidential)	2001	RH-287 Technical: Two-generation reproductive toxicity study in rats, Rohm and Haas Company, Report N° 99R-155,	Y(ii)	N	Rohm and Haas

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
			GLP, Unpublished.			
III-A6.12.2/01	Wooder M.	2001	Worker health incidents resulting from exposure to 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one (RH-287); Rohm and Haas Company, Report N° 01R-1083, Unpublished.	Y(ii)	N	Rohm and Haas
III-A6.12.6/01	xxx (confidential)	1988a	RH-287 Technical (in Petrolatum): 21-Day Cumulative Irritancy Assay in Humans; Essex Testing Clinic, Inc. (Panel N°. 87182), Rohm and Haas Company Report N° 88RC-0008, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.12.6/02	xxx (confidential)	1988b	RH-287 Technical (in Petrolatum): 21-Day Cumulative Irritancy Assay in Humans; Essex Testing Clinic, Inc. (Panel N°. 88164), Rohm and Haas Company Report N° 88RC-008A, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.12.6/03	xxx (confidential)	1990	RH-287 Technical (in Corn Oil): 21-Day Cumulative Irritation Test Assay in Humans; Essex Testing Clinic, Inc. (Panel N°. 91015), Rohm and Haas Company Report N° 90RC-251, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.12.6/04	xxx (confidential)	1990	RH-287 Technical (in Corn Oil): 21-Day Cumulative Irritation and Sensitization Patch Test Assay in Human Volunteers; McWill Research Laboratories, Inc. (Panel N°. 91015), Rohm and Haas Company Report N° 90RC-252, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.12.6/05	xxx (confidential)	1992	RH-287 Technical: Cumulative Irritation of Test Articles on Healthy Individuals; Essex Testing Clinic, Inc. (Panel N°s. 91137, 92004, 92025), Rohm and Haas Company Report N° 91RC-163 (reformatted as Report N°. 91RC-163A), Unpublished.	Y(i)	N	Rohm and Haas
III-A6.12.6/06	xxx (confidential)	1992	RH-287 Technical Repeat Insult Patch Test in Humans; Essex Testing Clinic, Inc. (Panel N°s. 92132, 92134), Rohm and Haas Company Report N° 92RC-086 (reformatted Report N°. 92RC-086B), Unpublished.	Y(i)	N	Rohm and Haas
III-A6.12.6/07	xxx (confidential)	1993	Report Addendum. Potential in RH-287 Sensitized Human Volunteers using RH-287, RH-886 and RH-893; Essex Testing Clinic, Inc., Verona, NJ (Panel N°. 92134.1), Rohm and Haas Company Report N° 92RC-086A, Unpublished.	Y(i)	N	Rohm and Haas
III-A6.12.6/08	xxx (confidential)	1994	Kathon 930: Comparative Dermal Reactivity, Essex Testing Clinic, Inc. (Panel N°. 93121), Rohm and Haas Company Report N° 93RC-201, Unpublished.	Y(i)	N	Rohm and Haas
III-	Marbo, M.	2001	Hydrolysis of ^{14}C RH-5287 at pH 4, 7,	Y(ii)	N	Rohm

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
A7.1.1.1.1/01			and 9 at 25 and 40°C; Rohm and Haas Company, Technical Report N° TR-01-012 (May 7, 2001), GLP, unpublished.			and Haas
III-A7.1.1.1.1/02	Jacobson A., Beshah K. and Guo I.	2004	Structural Confirmation of RH-287 Sulfonic Acid Metabolite; Rohm and Haas Company, Technical Report N° TR-04-017 (9 August 2004), GLP, Unpublished	Y(ii)	N	Rohm and Haas
III-A7.1.1.1.2/01	Kesterson A., Lawrence B., Lawrence L.J.	1990	Aqueous Photolysis of $^{13/14}$C RH-5287 in Natural Sunlight; PTRL East, Inc. Richmond, Kentucky, USA, PTRL Report N° 1303, Rohm and Haas Technical Report N° 34-90-73 (December 27, 1990), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.1.1.1.2/02	Mazza L.S.	1993a	Supplemental Study on the Aqueous Photolysis of 14C RH-5287 in Natural Sunlight, Supplemental to Rohm and Haas Technical Report N° 34-90-73; Rohm and Haas Company, Research Laboratories, Technical Report N° 34-92-98 (April 15, 1993), GLP, Unpublished	Y(i)	N	Rohm and Haas
III-A7.1.1.2.1/01	Seyfried B.	2003a	Ready Biodegradation of RH-25,287 in a CO_2 Evolution (Modified Sturm) Test; RCC Ltd. CH-4452 Itingen, Switzerland, RCC Study N°.: 847085, Rohm and Haas Report N° GLP-2003-053 (November 10, 2003), GLP, unpublished	Y(ii)	N	Rohm and Haas
III-A7.1.2.2.1/01	Guo I., Jacobson A., Eisenschmied M.	2004	Aerobic Transformation of RH-5287 in Surface Water; Rohm and Haas Technical Report N° GLP-2004-26 (December 20, 2004), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.1.2.2.2.a/01 and A7.1.2.2.2.b/01	Millais A.J.	2005	^{14}C-RH-5287 Degradability and Fate in the Water/Sediment System; Huntingdon Life Sciences Ltd., Cambridgeshire, U.K. HLS Report RAS 262/042008, Rohm and Haas Technical Report N° TR-05-093 (July 14, 2005), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.1.2.2.2.c/01	Lawrence L.J., Lawrence B., Jackson S. and Kesterson A.	1991	Aerobic Aquatic Metabolism of $^{13/14}$C RH-5287; PTRL East, Inc., Richmond, Kentucky, USA, PTRL Report Number 1291, Rohm and Haas Technical Report N° 34-91-01 (March 26, 1991), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.1.2.2.2.c/02	Kesterson A. and Atkins R.	1992a	Supplemental Study on the Aerobic Aquatic Metabolism of $^{13/14}$C RH-5287; PTRL East, Inc. Richmond, Kentucky, USA, PTRL Report Number 1291, Rohm and Haas Technical Report N° 34-92-13 (May 1, 1992), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.1.2.2.2.c/03	Mazza L.S.	1993b	Supplemental Study on the Aerobic Aquatic Metabolism of RH-5287; Rohm and Haas Company, Spring House, Pennsylvania, USA, Rohm and Haas Technical Report N° 34-93-31 (May 7, 1993), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.1.2.2.2.c/	Jacobson A.	1995	Extractability and Storage Stability of RH-5287 in Marine Sediment; Rohm and	Y(i)	N	Rohm and

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
04			Haas Company Technical Report N° 34-95-16.			Haas
III-A7.1.2.2.2.d/01	Lawrence L.J., Lawrence B. and Kesterson A.	1991	Anaerobic Aquatic Metabolism of $^{13/14}$C RH-5287; PTRL East, Inc., Richmond, Kentucky, USA, PTRL Report Number 1313, Rohm and Haas Technical Report N° 34-91-06 (March 21, 1991), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.1.2.2.2.d/02	Kesterson A. and Atkins R.	1992b	Supplemental Study on the Anaerobic Aquatic Metabolism of $^{13/14}$C RH-5287; PTRL East, Inc. Richmond, Kentucky, USA, PTRL Report Number 1313, Rohm and Haas Technical Report N° 34-92-46 (May 19, 1992), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.1.2.3/01	Seyfried B.	2003b	Ready Biodegradation of N-(n-octyl) Malonamic Acid in a CO_2 Evolution (Modified Sturm) Test; RCC Ltd, CH-4452 Itingen, Switzerland, RCC Study N°.: 847085, Rohm and Haas Report N° GLP-2003-033 (November 05, 2003), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.1.2.3/02	Seyfried B.	2003c	Ready Biodegradation of N-(n-octyl) Acetamide in a CO_2 Evolution (Modified Sturm) Test; RCC Ltd. CH-4452 Itingen, Switzerland, RCC Study N°.: 843970, Rohm and Haas Report N° GLP-2003-034 (November 05, 2003), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.1.2.3/03	Seyfried B.	2006	2-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid (monohydrate): Ready Biodegradabiity in a CO_2 Evolution (Modified Sturm) Test; RCC Ltd, CH-4452 Itingen, Switzerland, RCC Study No.: A42671, Rohm and Haas Report N° GLP-2006-030 (June 15, 2006), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.1.3.a/01	Swales S.	2002	^{14}C-RH-5287 Technical: Activated Sludge Adsorption Isotherm; Covance Laboratories Ltd., North Yorkshire England, Covance Report N°. 616/30-D2149, Rohm and Haas Report N° 02RC-0029 (December 23, 2002), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.1.3.b/01	Olson G.L. and Lawrence L.J.	1991a	Soil Adsorption/Desorption of ^{14}C RH-5287 by the Batch Equilibrium Method; PTRL East, Inc., Richmond, Kentucky, USA. PTRL Report N°. 1246, Rohm and Haas Technical Report N° 34-90-28 (January 2, 1991). Unpublished.	Y(i)	N	Rohm and Haas
III-A7.2.1/01	Reynolds J.L.	1999	Aerobic Soil Metabolism of ^{14}C RH-5287; Xenobiotic Laboratories, Inc (XBL), Plainsboro, New Jersey, USA, XBL Report N°. RPT00433, Rohm and Haas Technical Report N°. 99-01 (March 9, 1999), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.2.3.1/01	Olson G.L. and Lawrence	1991b	Leaching of $^{13/14}$C RH-5287 in Four Soil Types Following 30 Days or One Half-	Y(i)	N	Rohm

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
	L.J.		Life of Aerobic Aging in Sandy Loam Soil; PTRL East, Inc., Richmond, Kentucky, USA, PTRL Report N°. 1296, Rohm and Haas Technical Report N° 34-90-67 (January 30, 1991), GLP, Unpublished.			and Haas
III-A7.3.1/01	Guo I.	2003	Calculation of Tropospheric Phototransformation of Isothiazolone Compounds; Rohm and Haas Company, Rohm and Haas Technical Report N° TR-03-001 (May 15, 2003), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.1.1.a/01	xxx (confidential)	1990a	Acute flow-through toxicity of RH-287 technical to rainbow trout (*Salmo gairdneri*); ABC Laboratory Project ID: 37737, Rohm and Haas Report N° 89RC-0015 (March 8, 1990), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.1.1.a/02	xxx (confidential)	1990b	Acute flow-through toxicity of RH-287 technical to bluegill sunfish (*Lepomis macrochirus*); ABC Laboratory Project ID: 37736, Rohm and Haas Report N° 89RC-0016 (March 8, 1990), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.1.1.b/01	xxx (confidential)	1990a	Acute flow through toxicity of RH-287 to the sheepshead minnow, *Cyprinodon variegatus*; EnviroSystems Study N°: 8961-RH, Rohm and Haas Report N° 89RC-0262 (November 28, 1990), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.1.1.b/02	xxx (confidential)	1997	Acute toxicity test of RH-287 with Japanese blowfish; Department of Environmental Ecology, Institute of General Science for Environment, Shin-Nippon Meteorological and Oceanographical Consultant Co., Ltd, Test Number E001, Rohm and Haas Report N° 97RC-1028 (September 1997), Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.1.1.c/01	xxx (confidential)	1994a	Static acute toxicity of N-(n-octyl) malonamic acid to rainbow trout (*Oncorhynchus mykiss*) (metabolite); ABC Laboratories Project ID 41110, Rohm and Haas Report N° 93RC-0166 (July 7, 1994), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.1.1.c/02	xxx (confidential)	2002a	Acute toxicity of N-(n-octyl) acetamide to the Rainbow Trout, *Oncorhynchus mykiss*, determined under static test conditions (metabolite); ABC Laboratories Study N°: 47175, Rohm and Haas Report N° 01RC-297 (June 21, 2002), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.1.2.a/01	Burgess D.	1990	Acute flow-through toxicity of RH-287 technical to *Daphnia magna*; ABC Laboratories Project ID: 37738, Rohm and Haas Report N° 89RC-0017 (July 17, 1990), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.1.2.b/01	Boeri R.L. and Ward T.J.	1990	Acute flow through toxicity of RH-287 to the mysid, *Mysidopsis bahia*;	Y(i)	N	Rohm

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			EnviroSystems Study N°: 8962-RH, Rohm and Haas Report N° 89RC-0305 (November 28, 1990), GLP, Unpublished.			and Haas
III-A7.4.1.2.b/02	Roberts M.H., De Lisle P.F., Vogelbein M.A. and Hale R.C.	1990	Acute toxicity of RH-287 to the American oyster *Crassostrea virginica* in static natural and synthetic estuarine waters; Virginia Institute of Marine Science VIMS Study N°. 8805, Rohm and Haas Report N° 89RC-0037 (November 14, 1990), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A.7.4.1.2.b/03	Boeri R.L., Wyskiel D.C. and Ward T.J.	2001	(2001) RH-287 technical: bivalve acute toxicity test (embryo-larval) with the bay mussel, *Mytilus edulis*; TR Wilbury Study N°: 2195-RH, Rohm and Haas Report N° 01RC-0145 (November 9, 2001), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.1.2.c/01	Hahne R.	2002a	Acute toxicity of N-(n-octyl) malonamic acid, technical, PMN to the water flea, *Daphnia magna*, under static test conditions, (metabolite); ABC Laboratories Study N°: 47086, Rohm and Haas Report N° 01RC-0281 (May 22, 2002), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.1.2.c/02	Rhodes J.E.	2002b	Acute toxicity of N-(n-octyl) acetamide to the water flea, *Daphnia magna*, under static test conditions (metabolite); ABC Laboratories Study N°: 47174, Rohm and Haas Report N° 01RC-0298 (June 25, 2002), Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.1.3.a/01	Boeri R.L., Wyskiel D.C. and Ward T.J.	2002c	RH-287 Technical: growth and reproduction toxicity test with the freshwater alga, *Navicula pelliculosa*, TR Wilbury Study N°: 2199-RH, Rohm and Haas Report N° 01RC-0140 (April 10, 2002), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.1.3.a/02	Hughes C.	2002a	Toxicity of RH-287 technical to the unicellular green alga, *Selenastrum capricornutum*; ABC Laboratories Study N°: 47616, Rohm and Haas Report N° 02RC-0053 (September 13, 2002), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.1.3.a/03	Sindermann A.B., Kendall T.Z. and Krueger H.O.	2007	4,5-Dichloro-2-n-octyl-4-isothiazolin-3-one technical: A 96-hour toxicity test with the freshwater diatom (*Navicula pelliculosa*), Wildlife International Limited Project N° 129A-215, Rohm and Haas Report N° 06RC-175 (June 20, 2007), GLP, Unpublished	Y (ii)	N	Rohm and Haas
III-A7.4.1.3.b/01	Boeri R.L., Wyskiel D.C. and Ward T.J.	2002b	RH-287 Technical: growth and reproduction toxicity test with the marine alge, *Skeletonema costatum*; TR Wilbury Study N°: 2200-RH, Rohm and Haas Report N° 01RC-0141 (March 8, 2002), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.1.3.c/01	Hahne R.	2002b	Toxicity of N-(n-octyl) malonamic acid, technical, PMN to the unicellular green alga, *Selenastrum capricornutum*. (metabolite); ABC Laboratories Study	Y(ii)	N	Rohm and Haas

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			N°: 47087, Rohm and Haas Report N° 01RC-0279 (May 23, 2002), GLP, Unpublished.			
III-A7.4.1.3.c/02	Hahne R.	2002c	Toxicity of N-(n-octyl) malonamic acid, technical, PMN to the saltwater diatom, *Skeletonema costatum* (metabolite); ABC Laboratories Study N°: 47088, Rohm and Haas Report N° 01RC-0280 (March 14, 2002), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.1.3.c/03	Rhodes J.E.	2002c	Toxicity of N-(n-octyl) acetamide to the unicellular green alga, *Selenastrum capricornutum* (metabolite); ABC Laboratories Study N°: 47176, Rohm and Haas Report N° 01RC-0299 (April 1, 2002), GLP, Unpublished	Y(ii)	N	Rohm and Haas
III-A7.4.1.4	Ward T.J., Kowalski P.L. and Boeri R.L.	1997	Activated sludge respiration inhibition test with RH-287; TR Wilbury Laboratories Study N°: 1034-RH, Rohm and Haas Report N° 96RC-0129 (March 14, 1997), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.3.2.a/01	xxx (confidential)	2002d	Early life-stage toxicity of RH-287 technical to the rainbow trout (*Oncorhynchus mykiss*) under flow-through conditions; ABC Laboratories Study N°: 46578, Rohm and Haas Report N° 01RC-0137 (December 10, 2002), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.3.2.b/01	xxx (confidential)	1990b	Early life stage toxicity of RH-287 to the sheepshead minnow (*Cyprinodon variegatus*); EnviroSystems Study N°: 8913-RH, Rohm and Haas Report N° 89RC-0193 (November 30, 1990), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.3.3.1.a/01	xxx (confidential)	1985	Uptake, Depuration and Bioconcentration of ^{14}C RH-5287 by Bluegill Sunfish (*Lepomis macrochirus)*; ABC Laboratories, ABC Report N°.32970, Rohm and Haas Technical Report N° 310-86-33 (16 September 1985), Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.3.3.1.a/02	xxx (confidential)	1986a	Metabolite Characterization of RH-5287 in Bluegill Sunfish (*Lepomis macrochirus*); ABC Laboratories, ABC Report N°.32971, Rohm and Haas Technical Report N° 310-86-32 (20 March 1986), Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.3.3.1.a/03	xxx (confidential)	1986b	Metabolite Characterization of RH-5287 in Bluegill Sunfish (*Lepomis macrochirus*): A Supplemental Report to ABC Final Report N°. 32971; ABC Laboratories, ABC Report N°.32971-2, Rohm and Haas Technical Report N° TR-31S-86-36 (7 April 1987), Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.3.3.1.a/04	xxx (confidential)	1991	Metabolism of RH-5287 in Bluegill Sunfish; Rohm and Haas Company, Rohm and Haas Technical Report N° 34-90-71 (27 March 1991), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.3.3.1.b/	xxx (confidential)	1988a	Bioaccumulation Study of (^{14}C)-4,5-Dicholoro-2-n-octyl-isothiazolin-3-one	Y(i)	N	Rohm

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
01			(^{14}C-RH-287) with Carp (*Cyprinus carpio*); Mitsubishi-Kasei Institute of Toxicological and Environmental Sciences, MITES Report N°. 7A806G, Rohm and Haas Technical Report N° 88RC-1030 (26 December 1988), GLP, Unpublished.			and Haas
III-A7.4.3.3.1.b/02	xxx (confidential)	1988b	^{14}C-RH-287 in Water and ^{14}C-residue in fish tissues from a Bioconcentration Study; Mitsubishi-Kasei Institute of Toxicological and Environmental Sciences, MITES Report N°. 7A806G (2), Rohm and Haas Technical Report N° 88RC-1031 (26 December 1988), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.3.3.2/01	Ward T.J., Wyskiel D.C. and Boeri R.L.	2002	Bioconcentration Test with RH-287 Technical and the Oyster, *Crassostrea virginica*; T.R. Wilbury Laboratories, Inc, Study N°. 2197-RH, Rohm and Haas Report N° 01RC-0146 (October 4, 2002), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.3.4.a/01	Ward T.J. and Boeri R.L.	1990c	Chronic toxicity of RH-287 to the daphnid (*Daphnia magna*); EnviroSystems Study N°. 9031-RH, Rohm and Haas Report N° 90RC-0050 (November 30, 1990), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.3.4.b/01	Ward T.J. and Boeri R.L.	2000	RH-287: flow-through chronic toxicity to the mysid, *Americamysis bahia*; TR Wilbury Study N°: 1927-RH, Rohm and Haas Report N° 99RC-0197 (June 1, 2000), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.3.5.1a/01	Thomas S.T., Krueger H.O., Kendall T.Z. and Nixon W.B.,	2007	14C-4,5-Dichloro-2-n-octyl-4-isothiazolin-3-one: A survival and growth sediment toxicity test with *Chironomus tentans* (using spiked sediment); Wildlife International Limited Project N° 129A-210, Rohm and Haas Report N° 06RC-174 (June 4, 2007), Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.3.5.1.a/02	Aufderheide J.	2003	RH-287 Technical: Chronic toxicity in whole sediment to the freshwater midge, *Chironomus riparius*; ABC Laboratories Study N°: 47636, Rohm and Haas Report N° 02RC-0051 (October 1, 2003), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.3.5.1.b/01	Jones A. and Aufderheide J.	2003	RH-287 Technical: Chronic Toxicity in Whole Sediment to the Marine Amphipod, *Leptocheirus plumulosus;* ABC Laboratories Study N°. 47638, Rohm and Haas Report N° 02RC-0050 (October 2, 2003), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.4.3.5.1.b/02	Hughes C. and Aufderheide J.	2003	RH-287 Technical: chronic toxicity in whole sediment to the marine polychaete, *Neanthes arenaceodentata;* ABC Laboratories Study N°. 47637, Rohm and Haas Report N° 02RC-0052 (October 2, 2003), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.4.3.5.2/01	Rhodes J.E.	2002e	Toxicity of RH-287 technical to duckweed, *Lemna gibba* G3, determined	Y(ii)	N	Rohm

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
			under static test conditions; ABC Laboratories Study N° 47171, Rohm and Haas Report N° 01RC-0309 (July 2, 2002), GLP, Unpublished.			and Haas
III-A7.5.1.1/01	van der Kolk J.	2002	RH-287 technical: determination of the effects on soil microflora activity; Springborn Smithers Study N°: 1007.079.747, Rohm and Haas Report N° 01RC-0142 (January 15, 2002), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.5.1.2/01	Boeri R.L., Wyskiel D.C. and Ward T.J.	2002a	RH-287 Technical: acute toxicity to the earthworm, *Eisenia foetida*; TR Wilbury Study N°: 2201-RH, Rohm and Haas Report N° 01RC-0143 (February 28, 2002), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.5.1.3/01	Teixeira D.	2002a	RH-287 Technical – determination of effects on seedling emergence and seedling growth of three plant species; Springborn Smithers Study N°: 86.6244, Rohm and Haas Report N° 01RC-0144 (November 25, 2002), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.5.1.3/02	Teixeira D.	2002b	RH-287 Technical – determination of effects on vegetative vigor of three plant species; Springborn Smithers Study N°: 86.6245, Rohm and Haas Report N° 01RC-0144A (November 25, 2002), GLP, unpublished.	Y(ii)	N	Rohm and Haas
III-A7.5.2/01	Warbritton R.	2005	4,5-Dichloro-2-octyl-3(2H)-isothiazolone: survival, growth and reproduction test with the earthworm, *Eisenia fetida*; ABC Laboratories Study N°: 49174, Rohm and Haas Report N° 04RC-0069 (May 10, 2005), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III-A7.5.3.1.1/01	xxx (confidential)	1976a	Acute oral LD_{50} - mallard duck. RH-287, Wildlife International Project N°: 129-112; Rohm and Haas Report N° 76RC-1050 (September 23, 1976), Unpublished.	Y(i)	N	Rohm and Haas
III-A7.5.3.1.2/01	xxx (confidential)	1992a	RH-287 technical: 8-day acute dietary LC_{50} study in bobwhite quail; Bio-Life Associates BLAL # 111-001-01, Rohm and Haas Report N° 91RC-0016 (January 7, 1992), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III-A7.5.3.1.2/02	xxx (confidential)	1992b	RH-287 technical: 9-day acute dietary LC_{50} study in mallard ducklings; Bio-Life Associates BLAL # 111-002-02, Rohm and Haas Report N° 91RC-0017 (January 7, 1992), GLP, Unpublished.	Y(i)	N	Rohm and Haas

List of studies for the theoretical product

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
III B3/01 covering B3.1.1 B3.1.2 B3.1.3 B3.2 B3.5 B3.6 B3.7.2 B3.8 B3.10	Evans, J.A., Mullee, D.M.	2002	SEA-NINE™ 211 Marine Antifouling Agent: Determination of Physico-chemical properties. Safepharm Laboratories Ltd., Derby, U.K. , Rohm and Haas Company, Technical Report No. 1606/001 (11 June 2002), GLP, Unpublished	Y(ii)[10]	N	Rohm and Haas
III B3/02 covering B3.4	Tremain, S.P.	2005	SEA-NINE™ 211N Marine Antifouling Agent: Determination of Hazardous Physico-chemical properties. Safepharm Laboratories Ltd., Derby, U.K. Report N° 1606/017, Rohm and Haas Company, Technical Report No.GLP-2005-053 (20 october 2005), GLP, Unpublished	Y(ii)	N	Rohm and Haas
III B3/03 covering B3.7.1	Nagahashi, S.L.	2005	Biocidal Product Directive Common Core Dataset for Biocidal Products, Part B3, Section 3.7: Storage stability; Stability and Shelf Life (Accelerated storage stability of SEA-NINE™ 211N Marine Antifouling Agent, to CIPAC MT46. Rohm and Haas Company, Technical Report No.GLP-2005-055 (3 november 2005), GLP, Unpublished.	Y(ii)	N	Rohm and Haas
III B3/04 covering B3.7.3	Woolley, A.J. and Mullee, D.M.	2004	SEA-NINE™ 211 Marine Antifouling Agent: Determination of Storage stability and corrosion characteristics. Safepharm Laboratories Ltd., Derby, U.K. , Rohm and Haas Company, Technical Report No. 1606/003 (7 July 2004), GLP, Unpublished	Y(ii)	N	Rohm and Haas
III B4.1.a/01	Doshi D.R.	2005	CIS Test Method 04-93-02," Reverse Phase HPLC Analysis of SeaNine™ formulation for Active Ingredient 4,5-dichloro-n-octyl-4-isothiazolin-3-one (DCOI, DCOIT or RH-287), Rohm and Haas Company, Report N° TM04-93-02 (May 27, 2005), Unpublished.	Y(ii)	Y	Rohm and Haas
III B4.1.a/02	Berrios E.	2005	GLP Validation of CIS Test Method No. 04-93-02, "Reverse Phase HPLC Analysis of SeaNine™ formulation for Active Ingredient 4,5-dichloro-n-octyl-4-isothiazolin-3-one (DCOI, DCOIT or RH-287)" Rohm and Haas Company, Report	Y(ii)	N	Rohm and Haas

[10] Y(ii) : Data protection claimed in accordance with Article 12.1(c) (ii) : Active substance already on the market on 14 May 2000. Data submitted for the first time in support of the first inclusion in Annex I or IA or Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA (data generated after the entry into force of the Directive.).

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
			N°GLP-2005-016 (May 3, 2005), GLP, Unpublished.			
III B4.1.b/01	Marbo, M.	1994a	CIS Test Method 94-45-01," HPLC test method for percent level RH-287 in antifoulant paint", Rohm and Haas Company, Report N° TM94-45-01 (July 28, 1994), Unpublished.	Y(i)[11]	Y	Rohm and Haas
III B4.1.b/02	Marbo, M.	1994b	GLP validation of BRAG analytical test method 94-45-01," HPLC test method for percent level RH-287 in antifoulant paint" protocol 24P-94-010, Rohm and Haas Company, Report N° GLP-94-23 (October 31st, 1994), Unpublished.	Y(i)	Y	Rohm and Haas
III-B5.10/06	Cookson, L.J., Greaves, H	1987	Evaluation of the fungicidal effectiveness of isothiazolone; CSIRO (DCWT), Clayton, Victoria, Australia; No Report No.; Not GLP; Unpublished	Y(ii)	N	Rohm and Haas
III B6.1.1/01	xxx (confidential)	1989a	Antifoulant C-9211 HQ: acute oral toxicity study in male and female rats, Rohm and Haas Company, Rohm and Haas Report N°: 88R-224 (May 9, 1989), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III B6.1.2/01	xxx (confidential)	1989b	Antifoulant C-9211 HQ: acute dermal toxicity study in male and female rabbits; Rohm and Haas Company, Report N° 88R-225, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III B6.1.3/01	xxx (confidential)	1992	Kathon™ 930 biocide: acute inhalation toxicity study in rats; Rohm and Haas Company, Report N° 91R-072, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III B6.1.3/02	xxx (confidential)	1993	Kathon™ 930 biocide: evaluation of the upper airway irritation potential (RD_{50}), International Research and Development Corporation Project ID: 285-048, Rohm and Haas Report N°: 91RC-048 (August 10, 1993), GLP, Unpublished.	Y(i)	N	Rohm and Haas
III B6.2.a/01	xxx (confidential)	1989c	Antifoulant C-9211 HQ: skin irritation study in rabbits; Rohm and Haas Company, Report N° 88R-226, GLP, Unpublished.	Y(i)	N	Rohm and Haas
III B6.3/01	xxx (confidential)	1986	Anti-Foulant C-9211 HQ delayed contact hypersensitivity study in guinea pigs, Rohm and Haas Company, Rohm and Haas Report N°: 86R-067 (November 15, 1986), GLP, Unpublished	Y(i)	N	Rohm and Haas
III B6.4/01	Ward R.J.	2004	In Vitro Absorption of a biocide from marine antifoulant paint RH-1 through rat	Y(ii)	Y	Rohm and

[11] Y(i) : Data protection claimed in accordance with Article 12.1(c) (i) : Active substance already on the market on 14 May 2000. Data submitted to the MS before 14 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA (data already submitted in member states).

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
			and human epidermis, Central Toxicology Laboratory (CTL) Study N° JV1787, Cheshire, UK, Rohm and Haas Report N° 03RC-089, GLP, Unpublished.			Haas
III B6.4/02	de Ligt R.A.F.	2007	In vitro percutaneous absorption of [^{14}C]DCOIT formulated as Sigma Ecofleet 530 through human skin membranes using flow-through diffusion cells, TNO Project N° 031.11646, TNO Study Code 7378, Sponsor: SigmaKalon Marine and Protective Coatings B.V. (29 March 2007), GLP Unpublished	Y (ii)	Y	PPG Coatings Europe B.V.
III-B6.4/03	xxx (confidential)	2007	Absorption, distribution, and excretion of ^{14}C-DCOIT following dermal application to male rats, Covance Laboratories Study Identification 6457-121, CMS 82956A and 616/063, Rohm and Haas Report N° 06RC-163 (November 13, 2007), GLP, Unpublished	Y(ii)	N	Rohm and Haas
III-B6.4/04	Toner, F.	2007	The *In Vitro* percutaneous absorption of radiolabelled DCOIT through human skin, Charles River Laboratories Study N° 779419, Rohm and Haas Report N° 06RC-164 (November 5, 2007), GLP, Unpublished	Y(ii)	N	Rohm and Haas
NK III-B6.4/05	Crow, L.F., Toner, F. and Roper, C.S.	2005	The *in vitro* percutaneous absorption of [^{14}C]-DCOIT in the presence of an aqueous wood treatment solution through human skin, Inveresk (formally changed to Charles River Laboratories October 3, 2005) Report N° 25894, Inveresk Study N° 776287, Rohm and Haas Report N° 05RC-054 (October 28, 2005); GLP Unpublished	Y(ii)	N	Rohm and Haas
III B6.6.1/01	Doshi, D.	1998a	Analysis for RH-287 (C-9211) in Support of Hempel Ship Painting Trial Rohm and Haas Company Report N° B-98-050 (July 15, 1998), Unpublished.	Y(ii)	Y	Rohm and Haas
III B6.6.1/02	Rière, L.D.	1990	Protocol for Hempel's antifouling paint exposure assessment. Rohm and Haas Company Report N° LDR 90-103 (May 28, 1990), Unpublished.	Y(ii)	Y	Rohm and Haas
III B6.6.2/01	Doshi, D.	1998b	International ship painting trial RH-287 (Sea-Nine™ Biocide) exposure results; Rohm and Haas Company Report N° B-98-062 (August 20, 1998), Unpublished.	Y(ii)	Y	Rohm and Haas
III B6.6.3/01	Doshi, D.	2000	Determination of penetration of SeaNine™ 211 Antifouling Agent active ingredient (4,5-Dichloro-2-n-octyl-4-isothiazolin-3-one) through painter's gloves and coveralls using a modified ASTM F-739 method., Rohm and Haas Report N° TR-00-013 (15 June 2000),	Y(ii)	Y	Rohm and Haas

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report N°. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Study submitted for the first time for PT21 (Y/N)	Owner
			GLP, Unpublished.			
III B7.1.2/01	Jacobson A	2006	Determination of the leach rate from the Danish naval patrol boat, Søløven (Sea Lion), Rohm and Haas Company, Report No: TR-06-010 (January 19, 2006), Unpublished.	Y(ii)	Y	Rohm and Haas
III B7.1.3/01	Sinning, D.J.	2000	Leach rate of Hempel Globic SP-ECO 81900 Antifoulant Paint containing Sea Nine™ 211 Antifouling Agent; Case Consulting Laboratories Inc. Study Nr 920-07 (31 January 2000), GLP, Unpublished.	Y(ii)	Y	Rohm and Haas

List of studies for Hempel's Antifouling Globic 81900

Section No/ Reference No.	Author (s)	Year	Title Source Company, Report No. GLP (Un)Published	Data protection Claimed (Yes/ No)	Study submitted for the first time for PT21 (Y/N)	Owner
III B3.1, 3.4 and 3.6	Ramsay N	2005	Globic 81900, Physico-Chemical testing of Globic 81900. Inveresk Research, Tranent, Edinburgh, Inveresk Study No: 207277, Inveresk Report No: 24515 GLP Unpublished	Yes (first)	Y	Hempel A/S
III B3.7/01	Graz L D	2002	Quantification of D468 in 81900-51110 b/n 0085184. Analytical Laboratories of Hempel A/S, Copenhagen. Report number A02456-3, 06/12-2002 Not GLP Unpublished	Yes (first)	Y	Hempel A/S
III B3.7/03	Hempel A/S	2004	Laboratory Instruction RD-008 Stormer Viscosimeter - Measurement of Viscosity LAB-Info No. 515 Latest up-date December 2004	Yes (first)	Y	Hempel A/S
III B3.7/04	Hempel A/S	2005a	Laboratory Instruction RD-015 Sag Test LAB-Info No. 518 Latest up-date March 2005	Yes (first)	Y	Hempel A/S
III B3.7/05	Hempel A/S	2005b	Laboratory Instruction RD-016 Beck-Koller - Measurement of Drying Time LAB-Info No. 518 Latest up-date March 2005	Yes (first)	Y	Hempel A/S
III B3.8/01	Hempel A/S	2001	Storage stability test: Hempel's Antifouling Globic SP-ECO 81900-50220 Project number PR99070. Not GLP Unpublished	Yes (first)	Y	Hempel A/S
III B3.8/03	Hempel A/S	2005a	Laboratory Instruction RD-015 Sag Test LAB-Info No. 518 Latest up-date March 2005	Yes (first)	Y	Hempel A/S
III B3.10/01	Ramsay N	2005	Globic 81900, Physico-Chemical testing of Globic 81900. Inveresk Research, Tranent, Edinburgh, Inveresk Study No: 207277, Inveresk Report No: 24515 GLP Unpublished	Yes (first)	Y	Hempel A/S
III B4.1/01	Eng K	1999	Quantitative determination of Sea-Nine 211 and Cuprous Oxide in antifouling paints – method validation, Hempel Analytical Laboratory – A-lab, Report number A99389, December 1999 Not GLP Unpublished	Yes (first)	Y	Hempel A/S

III B4.1/02	Graz L D	2002	Quantification of D468 in 81900-51110 b/n 0085184. Analytical Laboratories of Hempel A/S, Copenhagen. Report number A02456-3, 06/12-2002 Not GLP Unpublished	Yes (first)	Y	Hempel A/S
III B5.10/01	Soria M	2005	81900-51110 Performance Report, Hempel Villanova, Barcelona – Lab R&D, Report number A02649RES-11, Project number A2931PES, Not GLP Unpublished	Yes (first)	Y	Hempel A/S
III B5.10/02	Arias S	1989	Tin-free Classic 7611 – 7633 – 7655 Formulation and testing, Hempel Villanova, Barcelona – Lab R&D, Report number BRD 88/32, Project number POL 6019, 27/01-1989 Not GLP Unpublished	Yes (first)	Y	Hempel A/S
III B5.10/01 and B5.10/02	Arias S	1990	Application of panels for static raft test. Hempel's Guideline method no. ES-023-AS / RES-03. Edition n^0: 1 Unpublished	Yes (first)	Y	Hempel A/S
III B5.10/01 and B5.10/02	Pyne S	1991	Fouling assessment of raft immersion panels in Spain and Singapore. Hempel's Guideline no. ES-025-AF / RES-6. Edition n^0: 1 Unpublished	Yes (first)	Y	Hempel A/S
III B6.1.1	xxx (confidential)	1999a	Globic SP-ECO 81900 Acute oral toxicity (limit) test in rats. Inveresk Research, Tranent, Edinburgh, Inveresk Study No: 571971, Inveresk Report No: 17011 GLP Unpublished	Yes (first)	Y	Hempel A/S
III B6.1.2	xxx (confidential)	1999b	Globic SP-ECO 81900 Acute dermal toxicity (limit) test in rats. Inveresk Research, Tranent, Edinburgh, Inveresk Study No: 571987, Inveresk Report No: 16995 GLP Unpublished	Yes (first)	Y	Hempel A/S
III B6.2.1	xxx (confidential)	1999c	Globic SP-ECO 81900 Primary Skin Irritation Test in Rabbits. Inveresk Research, Tranent, Edinburgh, Inveresk Study No: 571992, Inveresk Report No: 17060 GLP Unpublished	Yes (first)	Y	Hempel A/S
III B6.2.2	xxx (confidential)	1999d	Globic SP-ECO 81900 Acute Eye Irritation test in Rabbits. Inveresk Research, Tranent, Edinburgh, Inveresk Study No: 572006, Inveresk Report No: 17172 GLP Unpublished	Yes (first)	Y	Hempel A/S
III B6.3	xxx (confidential)	1999	Hempel's Antifouling Globic SP-81900 Magnusson Kligman Maximisation Test in Guinea Pigs. Inveresk Research, Tranent, Edinburgh, Inveresk Study No: 572011,	Yes (first)	Y	Hempel A/S

Section No/ Reference No.	Author (s)	Year	Title Source Company, Report No. GLP (Un)Published	Data protection Claimed (Yes/ No)	Study submitted for the first time for PT21 (Y/N)	Owner
			Inveresk Report No: 17126 GLP Unpublished			
III B7.1.1 (III B7.1.3 in R&H dossier)	Sinning, D.J.	2000	Leach rate of Hempel Globic SP-ECO 81900 Antifoulant Paint containing Sea Nine™ 211 Antifouling Agent; Case Consulting Laboratories Inc. Study Nr 920-07 (31 January 2000), GLP, Unpublished.	Yes	Y	Rohm and Haas
III B7.1.2	Soria M	2006	Sea Nine release from A/F paint. Test in static and dynamic Report number A3188RES. June 2006. Unpublished	Yes	Y	Hempel A/S
III B7.1.3 (III B7.1.2 /01 in R&H dossier)	Jacobson A	2006	Determination of the leach rate from the Danish naval patrol boat, Søløven (Sea Lion), Rohm and Haas Company, Report No: TR-06-010 (January 19, 2006), Unpublished.	Y(ii)	Y	Rohm and Haas