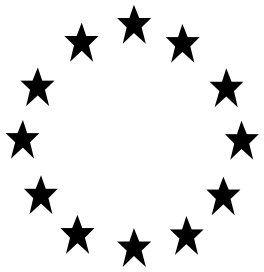
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment report



OIT

Product-type 8
(Wood preservatives)

October 2019

UK

CONTENTS

1 STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1 PROCEDURE FOLLOWED

This assessment report has been established as a result of the evaluation of the active substance OIT as product type 8 (wood preservatives), carried out in the context of Regulation (EU) No 528/2012, with a view to the possible approval of this substance.

On 27 April 2010, the UK competent authority received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 1 July 2010. The human health assessment was discussed at WGII 2014 and endpoints were agreed.

On 4 February 2016 the Rapporteur Member State submitted to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report (CAR).

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

1.2 PURPOSE OF THE ASSESSMENT REPORT

The aim of the assessment report is to support the opinion of the Biocidal Products Committee and a decision on the approval of OIT for product type 8, and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

2 OVERALL SUMMARY AND CONCLUSIONS

2.1 PRESENTATION OF THE ACTIVE SUBSTANCE

2.1.1 IDENTITY, PHYSICO-CHEMICAL PROPERTIES AND METHODS OF ANALYSIS

The main identification characteristics and the physico-chemical properties of OIT are given in Appendix I to this document.

Details of the methods of analysis supporting the batch analysis data are given in the confidential appendix. The method of analysis used to determine the active in the TGAI was quantitative NMR. While this method is acceptable to support the batch analysis data, a further fully validated method may be required for monitoring purposes as the use of quantitative NMR is not

a widely used technique and there is no specific reason in this case why only NMR had to be used. If such a method is required then it can be provided post approval of the active but prior to the date of entry into force.

HPLC-MS (single ion monitoring) methods have been validated for the determination of OIT in soil and water. The residue definitions for soil and water are OIT only.

The LOQ validated for soil complies with the relevant PNEC of 45 µg OIT/kg soil. As only a single ion was validated a confirmatory method is required. This can be provided post approval of the active but prior to the date of entry into force.

The LOQ validated for water complies with the EU drinking water directive and the NOEC of 0.38 µg/L. As only a single ion was validated a confirmatory method is required. This can be provided post approval of the active but prior to the date of entry into force.

A method is not required for air as the active is not sprayed and the VP is < 0.01 Pa.

Although OIT is classified as toxic a method for body fluids and tissues is not required as OIT dissipates rapidly in the body, OIT does not cause systemic toxicity and the metabolites observed are not regarded as of a concern.

The intended use pattern will not result in residues in food/feeding stuff and therefore methods for these commodities are not required.

2.1.2 INTENDED USES AND EFFICACY

OIT is an active substance proposed for use as a wood preservative (use classes 1and 2) in Product Type 8 of the Biocidal Products Regulation. OIT is a fungicide to be used in industrial pre-treatment of timber by vacuum pressure impregnation and dipping (manual and automated).

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

In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, and to apply adequately the provisions of Article 19 of Regulation (EU) No 528/2012 and the common principles laid down in Annex VI of that Regulation, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.3 CLASSIFICATION AND LABELLING

2.1.3.1 CURRENT ACTIVE SUBSTANCE CLASSIFICATION

The current harmonised classification of the active substance 2-octyl-2H-isothiazol-3-one (OIT) according to Regulation EC 1272/2008 is shown in Table 2.1.

Table 2.1 Current harmonised classification of OIT according to Regulation EC 1272/2008

Signal WORD:	Danger
Hazard class and category:	Acute Tox 3; Acute Tox 4; Skin Corr 1; Skin Sens 1; Aquatic acute 1; Aquatic chronic 1
Hazard statements:	H331 Toxic if inhaled H311 Toxic in contact with skin H302 Harmful if swallowed H314 Causes severe skin burns and eye damage H317 May cause an allergic skin reaction (specific concentration limit: C ≥ 0.05%) H400 Very toxic to aquatic life H410 Very toxic to aquatic life with long lasting effects

2.1.3.2 PROPOSED ACTIVE SUBSTANCE CLASSIFICATION

Based on the available data, the eCA proposal for classification of OIT according to Regulation EC 1272/2008 is shown in Table 2.2.

Table 2.2 Proposed classification of OIT according to Regulation EC 1272/2008

Signal WORD:	Danger
Hazard class and category:	Acute Tox. 3; Skin Corr. 1B; STOT SE 3; Skin Sens.1A; Aquatic acute 1; Aquatic chronic 1;
H-statements:	H301 Toxic if swallowed H311 Toxic in contact with skin H331 Toxic if inhaled H314 Causes severe skin burns and eye damage H335 May cause respiratory irritation H317 May cause an allergic skin reaction (specific concentration limit of C ≥ 0.005%) H400 Very toxic to aquatic life H410 Very toxic to aquatic life with long lasting effects

2.2 SUMMARY OF THE RISK ASSESSMENT

2.2.1 HUMAN HEALTH RISK ASSESSMENT

'ACTICIDE® OTW 8' is a biocidal product containing 8% w/w OIT which will be supplied as a concentrate and then diluted in a fully automated system with large amounts of water to form an on-site treatment solution with an in-use OIT concentration of 250 ppm (0.025% w/w OIT) for treatment of wood by dipping immersion and 150 ppm (0.015% w/w OIT) for treatment by vacuum-pressure impregnation.

It is used to treat freshly sawn timber against fungal growth during its service life (Class 2).

The toxicity associated with OIT is primarily a consequence of its local effects (corrosive and sensitising properties). Any indications of potential systemic toxicity observed in the experimental studies tend to be attributable to secondary consequences of local irritation/corrosion. However, a systemic assessment has been performed as it was not always clear whether the systemic effects observed in numerous studies were true systemic effects or just the consequence of the local toxicity of the substance.

2.2.1.1 HAZARD IDENTIFICATION

2.2.1.1.1 Toxicology Hazard Summary

For most endpoints, OECD test guideline compliant studies, usually conducted to GLP on either OIT or product formulations of OIT in propylene glycol, are available. Where guideline studies are not available, the non-submission is considered to be justified. Overall, there is no concern over the quality and extent of the data. In relation to the representative biocidal product, 'ACTICIDE® OTW 8', the assessment of its potential to cause adverse health effects is based on toxicity data for OIT, a skin irritation study on the product and on knowledge of the toxic properties of the co-formulants.

By the oral route OIT is extensively (up to around 70 % of administered dose) and rapidly absorbed following either single (in dose range 15 – 150 mg/kg bw/day) or repeated exposure (for dose levels of about 15 mg/kg bw/day). Oral absorption of 70 % was agreed at WGII 2014. By the dermal route absorption is less extensive, at about 40 % of administered dose for relatively low non-irritant concentrations of OIT (0.02 – 0.1%) in aqueous solution. Corrosive concentrations (> 5 % OIT; CLP generic concentration limit for corrosivity) were not tested, so it must be assumed that up to 100% of the administered dose could be absorbed at concentrations of OIT that cause corrosivity. The following were agreed at WGII 2014: 40 % for OIT in aqueous solution at low concentration [0.02 - 0.1 %]; 75% for concentrations 0.1 – 5 %; 100 % at corrosive concentrations (> 5 % OIT). No data are available for the inhalation route, but as OIT is extensively absorbed by the oral route, extensive systemic absorption following inhalation exposure (100%) can be predicted. Absorbed OIT is widely distributed throughout the body. OIT is completely metabolised both systemically and in the gastrointestinal tract by cleavage of the sulphur-nitrogen bond to open the isothiazolone ring. Both urine and bile are significant routes of excretion. Elimination is almost complete within 96 h. OIT and/or its metabolites show limited potential for bioaccumulation on repeated exposure. Because OIT is absorbed and widely distributed in the body, it can be predicted that transfer to the foetus, bone marrow and milk could occur.

On the basis of all the studies submitted, including those on the agreed LOEP, OIT is considered toxic via the oral (H301; LD_{50} 125 mg/kg), dermal (H311, LD_{50} 311 mg/kg) and the inhalation (H331; 4h LC_{50} 0.27 mg/l) routes. The current harmonised acute classification of OIT is Acute Tox 3 (H311-dermal, H331-inhalation) and Acute Tox 4 (H302 – oral). According to Regulation (EC) No 1272/2008, the biocidal product 'ACTICIDE® OTW 8' is classified as acute toxicity category 4 for the oral (H302, ATE_{mix} 1290 mg/kg) and inhalation routes (H332, ATE_{mix} 3.375 mg/l).

OIT is corrosive to skin and eyes (H314 Cat 1B), and is a respiratory tract irritant (H335). The current harmonised classification of OIT for this endpoint is Skin Corr 1B, H314. OIT is a very potent skin sensitiser (H317 Cat 1A), based on the observation of positive results in animal studies (see agreed LOEP). Dose response information indicates a risk of induction and elicitation at concentrations of about 100 ppm (0.01 %). This is broadly consistent with the harmonised classification of OIT for this endpoint (Skin Sens 1, H317) which stipulates a specific concentration limit for sensitisation of 500 ppm (0.05 %). WGII 2014) agreed an indicative human skin sensitisation NOAEC of 0.005 % (50 ppm) should be used wherever possible for semi-quantitative assessments of external dermal exposures. A potential for cross-sensitisation between OIT and other isothiazolins has also been demonstrated. The biocidal product, 'ACTICIDE® OTW 8', is also considered corrosive to skin and eyes (H314 Cat 1B), a respiratory tract irritant (H335) and a skin sensitiser (H317 Cat 1).

The main adverse effect of repeated oral exposure to OIT is local irritation of the stomach, observed in rat studies. The most sensitive oral NOAEC for medium-term and long-term exposure is 500 ppm in the diet, reported in an 18 month study in mice. There is no clear evidence of systemic toxicity in any of the studies; reduced bodyweight gain was observed in some studies, but this is likely to be secondary to local stomach irritation or due to poor palatability of test diets. The most sensitive oral NOAEL for systemic effects is 65 mg/kg bw/d identified from the 18-month dietary study in mice and based on reductions in body weight. Lower oral systemic NOAELs were identified for maternal toxicity in the gavage developmental rat toxicity study (5 mg/kg bw/d) and in the gavage rabbit developmental toxicity study (20 mg/kg bw/d); however, it is most likely the systemic effects (reductions in body weight and food consumption) observed in these studies were secondary to the local stomach irritation, which had been exacerbated by the method of test substance administration (gavage) employed in the studies. At WGII 2014 it was agreed that derivation of systemic AELs from these oral gavage NOAELs and extrapolation to systemic effects via the dermal and inhalation route would not be appropriate.

By the dermal route, repeated exposure to OIT causes local skin irritation of dose-related severity, as would be expected for a corrosive substance. A dermal NOAEC for local effects of 0.5 % (0.02 mg/cm^2) was identified in one 90-day study (6 h/day) in the rat, using a semi-occluded application site. An overall dermal NOAEC of 0.3 %, taken from the LOEP, for OIT local irritation on repeated exposure was agreed at WGII 2014. It should be noted however that skin sensitisation is the most sensitive dermal local effect, with an indicative human NOAEC of 0.005% (50 ppm). From the LOEP an overall NOAEL for systemic toxicity of 1.5 % (15 mg/kg/day) was identified (agreed at WGII 2014).

The applicant has not submitted data on the short-term or subchronic repeated exposure toxicity for the inhalation route, which for the reasons given is considered to be acceptable. A NOAEC is 0.64 mg/m^3 is taken from the LOEP agreed at WGII 2014.

OIT tested negative in valid *in vitro* gene mutation tests in bacteria and mammalian cells, and in an unsatisfactory *in vitro* clastogenicity test. OIT also tested negative in an *in vivo* clastogenicity test and an *in vivo* test for DNA damage/repair, demonstrating the absence of systemic genotoxic activity *in vivo*. Consequently, it is concluded that OIT is not an *in vivo* systemic mutagen. There are concerns about the thoroughness of the investigation for site of contact cytogenicity because the *in vitro* clastogenicity test, though negative, was unsatisfactory and *in vivo* tests addressing

this endpoint are not available. So, considering the reactivity of OIT at the initial site of contact, there are uncertainties as to whether OIT could express genotoxicity locally at the tissues of the initial site of contact and give rise to a carcinogenic response. However, it is concluded below that concerns for site of contact carcinogenicity are low given the risk management measures in place to protect against site of contact irritancy/corrosivity and sensitisation.

The potential carcinogenicity of OIT has been investigated in one long-term exposure study, in mice. On the basis of the lack of treatment-related tumours in this study, and taking account of absence of genotoxicity and systemic toxicity in other studies, it is concluded that the potential for OIT to cause systemic carcinogenicity is very low. However, it is possible tumours could be induced at sites of contact, via a proliferative mode of action due to the corrosivity/irritation of OIT, but the possibility of cancer via this potential mode of action is of low concern because risk management measures in place to protect against site of contact irritancy/corrosivity and sensitization will also protect against cancer.

No adverse effects on development were observed in standard developmental toxicity studies in the rat. Adverse effects on pregnancy and development, manifested as abortions and reduced foetal weight, were elicited in a standard rabbit developmental toxicity study, but this is considered to be a secondary non-specific consequence of maternal toxicity. Overall, there is no evidence that OIT is a specific developmental toxin. On the basis of the results of a standard 2-generation study, OIT does not have an adverse effect on fertility or reproductive performance.

Four of the five co-formulants in 'ACTICIDE® OTW 8' are not classified as dangerous with respect to human health and have no or limited potential for toxicity. The remaining co-formulant, present at 2.7 %, is classified as H302 (Harmful if swallowed) and H318 (Causes serious eye damage). No information is available on other possible hazardous properties for this co-formulant. Based on the available evidence there are no concerns in relation to mutagenicity, carcinogenicity or reproductive toxicity for 'ACTICIDE® OTW 8'.

2.2.1.1.2 Critical endpoints and derivation of AELs and AECs

The critical endpoints for OIT are driven by its local toxicity: skin sensitisation for the dermal route, respiratory tract irritation for the inhalation route and stomach irritation for the oral route. A local risk assessment is therefore required for these effects. Unspecific systemic effects are also seen with OIT but at much higher dose levels. In accordance with the most recent guidance (ECHA, 2013), systemic AELs will also be derived and a systemic risk assessment performed to supplement the local risk assessment.

Local effects

Oral

OIT causes local irritation of the stomach. The most sensitive oral NOAEC for medium-term and long-term exposure is 500 ppm in the diet, reported in an 18 month study in mice. As agreed at WGII 2014 no oral AEC for these local effects should be derived because the risk characterisation for possible local effects of OIT on the gastro-intestinal tract is most likely going to be covered by the systemic risk assessment.

Dermal

The most sensitive endpoint for the dermal route is skin sensitisation. In accordance with the most recent guidance (ECHA, 2013), a qualitative local dermal risk assessment will be performed for this critical endpoint. Information on the dose response relationship for skin sensitisation is available from the animal and human volunteer skin sensitisation studies, some of which are taken from the LOEP. The human and animal dose response information indicates a risk of induction and elicitation of skin sensitisation at concentrations of about 100 ppm and above and the human volunteer study suggests that that **50 ppm (0.005%)** could be an indicative human **NOAEC for skin sensitisation**; this dose response information will be used in a semi-quantitative local dermal risk assessment to supplement the qualitative one.

Inhalation

OIT causes local respiratory tract irritation of concentration related severity. The most sensitive NOAEC is 0.64 mg/m^3, taken from the LOEP agreed at WGII 2014.

To derive the AECs, an interspecies dynamic assessment factor (AF) of 2.5 has been applied as no interspecies toxicokinetic differences are expected because the mechanism of action appears to be simple, direct, irritation. To account for intraspecies differences, a default AF of 3.2 is used for toxicodynamic variability, but a factor for a toxicokinetic component is not necessary as the mode of action does not involve local metabolism. For the derivation of a long-term inhalation AEC an additional AF of 2 is required to extrapolate from a subchronic animal study to chronic human exposure.

The eCA believe that a reduction in inter- and intraspecies factors can be considered valid as the effect of OIT is a local dermal effect and locally on the respiratory tract. The UK considers that these local effects are absent of any metabolism or significant absorption differences. Please see source below from the 2014 WG on OIT:

"The eCA applied an interspecies assessment factor (AF) of 2.5 as no interspecies toxicokinetic differences were expected because the mechanism of action appears to be simple, direct, irritation; however, AF of 2.5 for possible toxicodynamic differences has been applied. To account for intraspecies differences, a default AF of 3.2 was used for toxicodynamic variability, but a factor for a toxicokinetic component was not necessary as the mode of action does not involve local metabolism.

FR considered the additional factor of 2 to extrapolate from subchronic to chronic exposure not adequate for local effects, highlighting that this type of effects is more concentration-dependent than time-dependent. According to the eCA, this type of effect is usually found to be more concentration-dependent, so that the eCA has proposed a relatively low AF of 2 to account for time extrapolation uncertainties."

Considering that the interspecies assessment factor was reduced to 2.5 at TOX WGII2014, given the effects of OIT are considered local and involve direct irritation, the same logic should be applied to the intraspecies assessment factor. As there is no toxicokinetic variability between individuals due to the mode of action not involving local metabolism the intraspecies assessment

factor should be reduced to 3.2, in line with the WG's decision on OIT's interspecies assessment factor.

The eCA does not have access to the study that underlies the AEC (from an OEL) that was established at the 2014 WG on OIT. Further support the removal of an assessment factor for a toxicokinetic component, can be found in the EPA registration document for Methylisothiazolinone (a member of the isothiazolone family, with the same mechanism of action), which reports that the chemical acts locally in acute, sub chronic and chronic toxicity studies with the corrosive properties of methylisothiazolinone imposing limitations on the dose levels (EPA, 1998 https://archive.epa.gov/pesticides/reregistration/web/pdf/3092.pdf). Considering the strong evidence supporting the any toxic effects of isothiazolone being local in nature and following the guidance on IR+CSA Chapter R.8.4.3.1 "since local effects are independent of the basal metabolic rate, allometric scaling should not be applied". This document can be found at https://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf .

Text from a review of isothiazolone biocides (of which OIT is a member) reports that they utilize a two-step mechanism to kill microbes. This involves rapid inhibition of growth and metabolism in the first minutes of contact followed by the irreversible damage of cells resulting in the loss of viability in the following hours (Wiliams., 2007). Isothiazolones are known to react with nucleophilic materials. This interaction affects their stability in the presence of reducing agents in addition to defining their mechanism of action with critical cell reaction sites. Thiols are key active sites on many proteins and enzymes in bacteria and mammalian cells. Research has shown that all isothiazolones react with protein thiols destroying both soluble and insoluble types. It has been postulated that this reactivity may be linked to the killing effect of isothiazolones with very few cells surviving the loss of thiols following contact with the biocide. Following the interaction of the isothiazolone with the thiol , the ring of the biocide opens and is no longer active, see figure 1 below. The direct effect of isothiazolones to induce cytotoxicity, in the absence of metabolism or absorption, highlights both the local effect of the biocide and also the reduction in potential for variability in response. Please see http://www.ppchem.com/free/ppchem-01-2007-2.pdf for further information on Isothiazolone's mode of action.

Thus, a **medium-term inhalation AEC of 0.08 mg/m^3** is derived by applying AFs of 2.5 x 3.2 to the animal NOAEC of 0.64 mg/m^3. No suitable acute inhalation toxicity data are available so a **short-term inhalation AEC of 0.08 mg/m^3**, is derived, using the medium-term inhalation AEC as a worst-case estimate.

A **long-term inhalation AEC of 0.04 mg/m^3** is derived by applying AFs of 2.5 x 3.2 x 2 to the animal NOAEC of 0.64 mg/m^3.

All AECs were agreed at WGII 2014 and confirmed at WG III 2016.

It should be noted that an uncertainty remains in applying these inhalation AECs derived from testing OIT in propylene glycol to the risk assessment of inhalation exposures to OIT from 'ACTICIDE® OTW 8' and its aqueous dilutions.

Systemic effects

There is no clear evidence of systemic toxicity in any of the available repeated dose studies; reduced bodyweight gain was observed in some studies, but this is likely to be secondary to local irritation. The most sensitive oral NOAEL for systemic effects is 65 mg/kg bw/d identified from the 18-month dietary study in mice and based on reductions in body weight. A lower oral systemic NOAEL was identified for maternal toxicity in the gavage rabbit developmental toxicity study (20 mg/kg bw/d); however, it is most likely the systemic effects (reductions in body weight and food consumption) observed in these studies were secondary to the local stomach irritation, which had been exacerbated by the method of test substance administration (gavage) employed in the studies. At WGII 2014 it was agreed that derivation of systemic AELs from these oral gavage NOAELs and extrapolation to systemic effects via the dermal and inhalation route would not be appropriate.

There is no evidence that OIT causes systemic toxicity by the dermal route in any of the groups treated for 3 months in the rat study. The applicant has not submitted data on the short-term or subchronic repeated exposure toxicity for the inhalation route, which for the reasons given is considered acceptable.

Overall, the most appropriate and critical systemic NOAEL for the derivation of systemic AELs is the NOAEL of 15 mg/kg bw/d (1.5 %) identified from a dermal rat 90-day study (taken from the LOEP agreed at WGII 2014 for PT6; Bernacki H.J. and Hamilton J.D. 1991; (A6.4.2/01 of PT6) Rohm and Haas Company Report Number 90R-031.). Adjusting this NOAEL for a dermal absorption value of 75 % and by applying a 100-fold assessment factor (AF), a **medium-term AEL of 0.11 mg/kg bw/d** is derived. No suitable short-term repeated dose toxicity data are available so a **short-term AEL of 0.11 mg/kg bw/d** is derived, using the medium-term AEL as a worst-case estimate. A **long-term AEL of 0.056 mg/kg bw/d** is derived by applying an additional AF of for subchronic-to-chronic extrapolation. These AELs were agreed at WGII 2014 and confirmed at WGIII 2016.

Table 2.3 Summary of critical endpoints and dose response information

Critical endpoint	Local AEC values		
	Short-term	**Medium-term**	**Long-term**
Stomach irritation	Oral AEC not Derived		
Skin sensitisation	Dermal AEC not relevant; qualitative risk characterisation performed supplemented by semi-quantitative approach with indicative human **NOAEC of 50 ppm (0.005%)**.		
Respiratory tract irritation	**$AEC_{inhalation}$ 0.08 mg/m^3**	**$AEC_{inhalation}$ 0.08 mg/m^3**	**$AEC_{inhalation}$ 0.04 mg/m^3**
Systemic effects (based on 90d dermal rat study)	**AEL = 0.11 mg/kg bw/day**	**AEL = 0.11 mg/kg bw/day**	**AEL = 0.056 mg/kg bw/day**

2.2.1.2 EXPOSURE ASSESSMENT

OIT is intended to be used as an active substance in wood preservatives. OIT is considered in this assessment for use in industrial pre-treatment of timber by vacuum pressure impregnation and automated dipping. 'ACTICIDE® OTW 8' is the representative biocidal product which contains 8 % w/w (80,000 ppm) OIT.

Table 2.6 presents the human exposure paths for OIT. These exposure estimates cover the entire lifecycle of 'ACTICIDE® OTW 8' where human exposure might take place during use of product and of treated products. Non-professional use of 'ACTICIDE® OTW 8' is not intended and no calculations for such exposure have been made.

Table 2.4 Summary of PT 8 applications and relevant routes of exposure for potential direct human contact to treated end-use products

Exposure path	Industrial (treatment of timber)	Professional (treatment of timber & use of treated products)	General public (use of treated products)
Inhalation	Yes	Yes	Yes
Dermal	Yes	Yes	Yes
Oral	No	No	Yes (infants)

2.2.1.2.1 Primary exposure

'ACTICIDE® OTW 8' is a biocidal product containing 8 % w/w (80,000 ppm) OIT which will be supplied as a concentrate and then diluted in a fully automated system with large amounts of water to form an on-site treatment solution with an in-use OIT concentration of 250 ppm (0.025 % w/w OIT) for treatment of wood by fully automated dipping and 150 ppm (0.015 % w/w OIT) for treatment by vacuum-pressure impregnation. It is used to treat freshly sawn timber against fungal growth during its service life (Class 2).

During and after treatment of timber with OIT-containing wood preservatives industrial/professional operator contamination could occur via the dermal, inhalation and oral routes. The potential for exposure of operators through ingestion of OIT during the industrial/professional uses is considered negligible.

The modelling of exposures and subsequent risk characterisation during production and formulation of 'ACTICIDE® OTW 8' is addressed under other EU legislation (e.g. Directive 98/24/EC) and not repeated under Regulation (EU) No. 528/2012 (agreed at Biocides Technical meeting TMI 2006). It was agreed at TMII 2006 (Arona,19-22 June 2006) that these data should not be routinely considered as a core requirement for the purposes of Annex I inclusion, so the above information is included for information only.

The activities of industrial users are:

- pre-application: mixing and loading – dilution of concentrates and transfer of liquids;

- application – including mixing/loading: fully automated dipping of wooden articles such as fence panels;
- vacuum pressure impregnation of timber;
- cleaning out dipping tank after use and,
- handling of wet treated wood.

Industrial operators handling the biocidal product (8 % w/w OIT concentrate) through a fully automated process must take extreme care to avoid spilling any product on their skin. In such conditions it may be assumed that dermal exposure would occur only in accidental circumstances. Due to the corrosive nature of OIT and the potential for skin sensitisation, typical PPE for an operator as recommended by the MSDS requires the use of chemical protective gloves, boots, eye protection and protective clothing whenever the material is handled and appropriate respiratory protection if airborne concentrations are not maintained. The MSDS states that skin cream should be used for skin protection and workers should be provided with a skin protection plan. The MSDS should also recommend that any facilities storing or utilizing OIT be equipped with an eye wash station and that local exhaust ventilation (LEV) be used as an engineering control where dust or mist evolution is possible.

2.2.1.2.2 Secondary exposure

Secondary exposures to OIT occur as a result of OIT-treated timber being used in areas accessible to the general public. Treated timber is used where weather resistance is required and exposure occurs for instance in house building. It is also conceivable that treated timbers are used to construct children's climbing frames and scenarios have been modelled to address this possibility.

The only relevant secondary exposure scenario identified in a professional setting would be sanding of OIT-treated wood. However, a number of secondary exposure scenarios have been identified for the general public and in a non-professional setting (non-professional sanding OIT-treated wood, infants playing on playground OIT-treated wood structures, infants chewing OIT-treated wood off-cut and exposure to volatilised residues from indoor OIT-treated timber).

It should be noted that for infants chewing OIT-treated wood off-cut (exposure via the oral route), only the systemic dose has been estimated as no oral AEC for local effects in the gastro-intestinal tract has been established. It was agreed at WGII 2014 that the risks of oral local irritative effects will be covered by the systemic risk assessment.

Wood treated with OIT-containing biocidal product is not intended for and should contain label restrictions against use in areas where it could come into contact with food e.g. food for human consumption is prepared, consumed or stored, or where the feedingstuff for livestock is prepared, consumed or stored.

2.2.1.2.3 Combined exposure

Not relevant.

2.2.1.3 RISK CHARACTERISATION

The critical endpoints for OIT are driven by its local toxicity: skin sensitisation for the dermal route, respiratory tract irritation for the inhalation route and stomach irritation for the oral route. A local risk assessment is therefore required for these effects. Unspecific systemic effects are also seen with OIT but at much higher dose levels. In accordance with the most recent guidance (ECHA, 2013), systemic AELs have also been derived and a systemic risk assessment performed to supplement the local risk assessment.

2.2.1.3.1 Primary exposure

Risk characterisation for systemic effects

The total systemic primary exposures estimated at Tier 1 and Tier 2 for the different industrial scenarios have been compared with the relevant AEL values in Table 2.5 below.

Table 2.5 Systemic risk characterisation for industrial primary exposure

Scenario	Tier	Total systemic dose [mg a.s./kg bw/day]	AEL [mg/kg bw/d]	Percentage of exposure/AEL	Acceptable risk [Y/N]
Mixing & loading (coupling/uncoupling transfer lines) (long-term)	**Tier 1** - no protection	negligible	0.056	N/A	Y
	Tier 2 - coveralls (10 % pen), gloves and boots	negligible	0.056	N/A	Y
Automated dipping (long-term)	**Tier 1 -** gloves and boots	0.0161	0.056	29%	Y
	Tier 2 - coveralls (10 % pen), gloves and boots	0.0032	0.056	6%	Y
Vacuum-pressure impregnation (long-term)	**Tier 1 –** gloves and boots	0.029	0.056	52%	Y
	Tier 2 - coveralls (10 % pen), gloves and boots	0.0059	0.056	11%	Y
Cleaning dip	**Tier 1 –** gloves	0.0161	0.056	29%	Y

tank (long-term)	and boots				
	Tier 2 - coveralls (10 % pen), gloves and boots	0.0032	0.056	6%	Y
Handling treated wet wood (long-term)	**Tier 1 –** gloves and boots	0.0161	0.056	29%	Y
	Tier 2 - coveralls (10 % pen), gloves and boots	0.0032	0.056	6%	Y

As shown by the table, risks of systemic effects in all the primary scenarios considered (coupling/uncoupling transfer lines, automated dipping, vacuum-pressure impregnation, cleaning dip-tank and handling treated wet wood) are acceptable even at Tier.

Risk characterisation for local effects

Inhalation

For local irritative effects on the respiratory tract, the primary inhalation exposures estimated at Tier 1 and Tier 2 for the different industrial scenarios have been compared with the relevant inhalation AEC values in Table 2.6 below.

Table 2.6 Local (respiratory) risk characterisation for industrial primary inhalation exposure

Scenario	Tier	Inhalation exposure concentration [mg/m^3]	Inhalation AEC [mg/m^3]	Percentage of exposure/inhalation AEC	Acceptable risk [Y/N]
Mixing & loading (coupling/uncoupling transfer lines) (long-term)	**Tier 1** – no protection	negligible	0.04	negligible	Y
	Tier 2 – coveralls (10 % pen), gloves and boots	negligible	0.04	negligible	Y
Automated dipping (long-term)	**Tier 1 –** gloves and boots	negligible	0.04	negligible	Y
	Tier 2 - coveralls (10 % pen), gloves	negligible	0.04	negligible	Y

	and boots				
Vacuum-pressure impregnation (long-term)	**Tier 1 –** gloves and boots	0.0003	0.04	0.75%	Y
	Tier 2 - coveralls (10 % pen), gloves and boots	0.0003	0.04	0.75%	Y
Cleaning dip tank (long-term)	**Tier 1 –** gloves and boots	negligible	0.04	negligible	Y
	Tier 2 - coveralls (10 % pen), gloves and boots	negligible	0.04	negligible	Y
Handling treated wet wood (long-term)	**Tier 1 –** gloves and boots	negligible	0.04	negligible	Y
	Tier 2 - coveralls (10 % pen), gloves and boots	negligible	0.04	negligible	Y

As shown by the table, inhalation exposures to OIT in all industrial scenarios are very low even at Tier 1, leading to acceptable risks of local irritative effects on the respiratory tract.

Dermal

The critical local dermal effect of OIT is skin sensitisation. For these effects, the in-use concentration of OIT in the different industrial scenarios has been compared with the indicative human NOAEC for skin sensitisation of 50 ppm. This semi-quantitative assessment is presented in Table 2.7 below. It should be noted that the dermal loading models do not differentiate between external exposure concentrations with or without protective gloves.

Table 2.7 Local (dermal skin sensitisation) semi-quantitative risk characterisation for industrial primary exposure

Scenario	In-use external concentration in contact with skin [ppm]	Indicative NOAEC for skin sensitisation [ppm]	Acceptable risk [Y/N]
Mixing & loading (coupling/uncoupling transfer lines)	80,000	50	N

(long-term)			
Automated dipping (long-term)	250	50	N
Vacuum-pressure impregnation (long-term)	150	50	N
Cleaning dip tank (long-term)	250	50	N
Handling treated wet wood (long-term)	250	50	N

As shown by the table, the in-use concentration of OIT in all primary scenarios is higher than the indicative NOAEC for skin sensitisation of 50 ppm. This would indicate an unacceptable risk of skin sensitisation in all scenarios. However, it should be noted that in this semi-quantitative assessment, it is not possible to quantify the effects of PPE or other risk mitigation measures. Therefore, in line with the most recent guidance (ECHA, 2013), a qualitative assessment is performed (see below).

Table 2.8 Qualitative risk characterization for local effects (skin sensitization and corrosivity) for primary industrial scenarios

Mixing & Loading (Coupling/uncoupling transfer lines) – 8% (80,000 ppm) OIT										
Hazard			**Exposure**							**Risk**
Hazard Category	**Effects in terms of C&L of the product**	**Additional relevant hazard information**	**PT**	**Who is exposed?**	**Tasks, uses, processes**	**Potential exposure route**	**Frequency and duration of potential exposure**	**Potential degree of exposure**	**Relevant RMM&PPE**	**Conclusion on risk**
Very High	Skin Sens 1 with 'extreme' potency[$] + Skin Cor 1	Indicative human NOAEC = 50 ppm	8	Industrial users	Dilution of concentrate (8% OIT) through automated process – exposure can arise from coupling/uncoupling of transfer lines	Skin, eyes, respiratory tract	Applicant informs one a day (15 min)	Incidental	**Personal protective equipment** • Respiratory protection • Hand protection (chemical-resistant gloves and barrier cream) • Eye protection (safety goggles) • Body protection (coated coveralls) **Engineering controls** The process is fully automated.	**Acceptable:** Engineering controls: automation; Low frequency; Minimization of manual phases; Professionals using PPE; Professionals following instructions for use; Good standard of personal hygiene.
Fully automated dipping – 0.025% (250 ppm) OIT										
Medium	Skin Sens 1 with 'moderate' potency*	Indicative human NOAEC = 50 ppm	8	Industrial users	Treated wet timber (0.025% OIT) is manually handled only when tension straps fail	Skin	Once a day (max 2 hr/day according to BPR guidance	Incidental	**Personal protective equipment** • Hand protection (chemical-resistant gloves) • Body protection (coated coveralls)	**Acceptable:** Engineering controls: automation;

							excel database)		**Engineering controls:** The process is automated.	Low frequency; Minimization of manual phases; Professionals using PPE; Professionals following instructions for use; Good standard of personal hygiene.
Vacuum-pressure impregnation – 0.015% (150 ppm) OIT										
Medium	Skin Sens 1 with 'moderate' potency*	Indicative human NOAEC = 50 ppm	8	Industrial users	Loading of untreated wood and removal of treated (0.015% OIT) wet wood	Skin	3 times a day (max 1 hour according to BPR guidance excel database)	-	**Personal protective equipment** • Hand protection (chemical-resistant gloves) • Body protection (coated coveralls) **Engineering controls:** Manual phases are minimized	**Acceptable:** Low frequency; Minimization of manual phases; Professionals using PPE; Professionals following instructions for use; Good standard of personal hygiene.
Cleaning dip tank – 0.025% (250 ppm) OIT										
Medium	Skin Sens 1 with 'moderate'	Indicative human NOAEC = 50	8	Industrial users	Cleaning dip tank	skin	Applicant informs once a	-	**Personal protective equipment**	**Acceptable:** Low frequency;

	potency*	ppm					week (30-60 min)		• Hand protection (chemical-resistant gloves) • Body protection (coated coveralls)	Professionals using PPE; Professionals following instructions for use; Good standard of personal hygiene.
Handling treated wet wood – 0.025% (250 ppm) OIT										
Medium	Skin Sens 1 with 'moderate' potency*	Indicative human NOAEC = 50 ppm	8	Industrial users	Handling occasionally treated wet wood	skin	Assumed max twice a week for 20 min	-	**Personal protective equipment** • Hand protection (chemical-resistant gloves) • Body protection (coated coveralls)	**Acceptable:** Low frequency; Professionals using PPE; Professionals following instructions for use; Good standard of personal hygiene.

$ A solution containing 80,000 ppm OIT (extreme sensitiser) is classified with Skin Sens 1 and it is considered to be of extreme potency. Such solution can therefore be assigned to the very high hazard category in line with ECHA (2013) guidance.
*Although the harmonised C&L of OIT has a SCL of 500 ppm for skin sensitisation, the eCA is of the view that a more appropriate SCL for this endpoint would be 50 ppm. On this basis, a solution containing 250 or 150 ppm OIT (extreme sensitiser) should be classified with Skin Sens 1 but it should be considered to be of moderate potency as it only contains a very small amount (150 or 250 ppm) of an extreme sensitiser . These solutions can therefore be assigned to the medium hazard category in line with ECHA (2013) guidance.

As shown by Table 2.8, risks of local sensitising effects on the skin and corrosivity are considered to be acceptable for the mixing and loading scenario (coupling and uncoupling transfer lines) where the concentrate product is handled (8% OIT) only when extensive PPE (respiratory protection, gloves, coveralls and eye protection) and engineering controls (full automation) are used. For the other scenarios, where the diluted product (150-250 ppm OIT) is handled, risks of local skin sensitising effects are considered to be acceptable through the use of appropriate PPE (gloves and coveralls), minimisation of manual phases (where possible) and good hygiene practice.

2.2.1.3.2 Secondary exposure

Risk characterisation for systemic effects

The total systemic exposure estimated for the different secondary scenarios has been compared with the relevant AEL value in Table 2.9 below.

Table 2.9 Systemic risk characterisation for secondary exposure scenarios

Scenario	Tier	Total systemic dose [mg a.s./kg bw/day]	AEL [mg/kg bw/d]	Percentage of exposure/AEL	Acceptable risk [Y/N]
Professional sanding OIT-treated wood (long-term)	**Tier 1** – no protection	0.00076	0.056	1.3%	Y
	Tier 2 – gloves	0.00016	0.056	0.3%	Y
Non-professional sanding OIT-treated wood (short-term)	**Tier 1** – no protection	0.00069	0.11	0.6%	Y
	Tier 2 – gloves	0.00008	0.11	0.07%	Y
Infants chewing OIT-treated wood (short-term)	**Tier 1 –** no protection	0.0084	0.11	8%	Y
Inhalation exposure of volatilised residues from indoor OIT-treated timber (long-term)	**Tier 1** – unventilated room	0.217 (toddler)	0.056	387.5%	N
	Tier 2 – ventilated room (constant rate model)	0.0371 (toddler)	0.056	66%	Y
	Tier 2 –	0.195	0.056	348%	N*

	ventilated room (evaporation model)	(toddler)			
Infants playing on playground OIT-treated wood structures (long-term)	**Tier 1 –** contact with 1 cm outer layer	0.0065	0.056	12%	Y
	Tier 2- contact with 1 mm outer layer	0.00065	0.056	1.2%	Y

As shown by the table above, risks of systemic effects for a number of secondary exposure scenarios at Tier 1 (professional and non-professional sanding OIT-treated wood, infants playing on playground OIT-treated wood structures and infants chewing OIT-treated wood off-cut) are acceptable. For exposure to volatilised residues from indoor OIT-treated timber, risks of systemic effects are unacceptable at Tier 1 when no ventilation is assumed. However, when more realistic conditions (ventilated room) are taken into account, acceptable risks are identified using the constant rate model.

* An alternative estimate of exposure to volatilised residues from indoor OIT-treated timber using the ConsExpo evaporation model predicts an unacceptable level of systemic exposure with ventilation. However, this model predicts a high mean event concentration of 0.23 mg/m^3 based on a high initial release rate. Although this worst case approach is considered relevant for assessing acute, local inhalation effects it is not considered valid for assessing systemic, repeated exposure.

Risk characterisation for local effects

Inhalation

For local irritative effects on the respiratory tract, the inhalation exposure estimated for the relevant secondary scenarios (professional and non-professional sanding OIT-treated wood and exposure to volatilised residues from indoor OIT-treated timber) has been compared with the relevant inhalation AEC value in Table 2.10 below.

Table 2.10 Local (respiratory) risk characterisation for secondary inhalation exposure

Scenario	Tier	Inhalation exposure concentration [mg/m^3]	Inhalation AEC [mg/m^3]	Percentage of exposure/inhalation AEC	Acceptable risk [Y/N]
Professional sanding OIT-treated wood (long-term)	**Tier 1** – no protection	0.00075	0.04	1.9%	Y
Non-professional	**Tier 1** – no	0.00075	0.08	0.9%	Y

sanding OIT-treated wood (short-term)	protection				
Inhalation exposure of volatilised residues from indoor OIT-treated timber	**Tier 1** – unventilated room	0.27	0.04	675%	N
	Tier 2 – ventilated room (0.6 ACH) Constant rate model (long term)	0.046	0.04	115%	N*
	Tier 2 – ventilated room (0.6 ACH) Evaporation model (short term)	0.244	0.08	305%	N**

As shown by the table, risks of local irritative effects on the respiratory tract are acceptable for professionals and non-professionals sanding OIT-treated wood. For exposure to volatilised residues from indoor OIT-treated timber, risks of local respiratory effects are unacceptable at Tier 1 (when no ventilation is assumed) and at Tier 2.

*Although the Tier 2 calculation of exposure to volatilised residues indoors using the constant rate model predicts unacceptable exposure levels for local effects, it is noted that this calculation is based on the unrealistic worst case scenario that the active substance will be released over a year and that an individual will be exposed for 24 hours/day, every day throughout this period.

** The Tier 2 calculation of exposure to volatilised residues indoors using the evaporation model is based on a high initial release rate resulting in a high mean event concentration of 0.23 mg/m^3. Although this calculation predicts an unacceptable exposure level for local effects, it is noted that the emission from solid matrices like wood is not perfectly described by the ConsExpo tool which overestimates the diffusion of the active substance through the wood. It is also noted that this calculation predicts that air levels will drop to zero after approximately 1.5 months meaning that the substance is totally depleted from the wood over this short period, which would seem unlikely in terms of product efficacy. In reality, the preservative is not applied on site but as a pre-treatment and, following application, the treated timber is dried and stored at the treatment site before being transported to a builder's merchant and stored again until purchase by the end user. The calculated initial peak in the emission from newly treated timber is therefore unlikely to result in the air concentrations predicted by the model when installed in domestic rooms.

Dermal

The critical local dermal effect of OIT is skin sensitisation. For these effects, the estimated concentration of OIT in the treated wood in the relevant secondary scenarios has been compared with the indicative human NOAEC for skin sensitisation of 50 ppm. This semi-quantitative assessment is presented in Table 2.11 below.

Table 2.11 Local (dermal skin sensitisation) semi-quantitative risk characterisation for secondary <u>dermal</u> exposure

Scenario	Tier	Concentration of OIT in treated wood in potential contact with skin [ppm]	Indicative NOAEC for skin sensitisation [ppm]	Acceptable risk [Y/N]
Professional sanding OIT-treated wood (long-term)	**Tier 1** – no protection	149.6	50	N*
	Tier 2 – assuming a transfer efficiency of 2 % for rough-sawn wood (TNsG 2002, Part 2, p. 206)	2.99	50	Y
Non-professional sanding OIT-treated wood (short-term)	**Tier 1** – no protection	149.6	50	N*
	Tier 2 – assuming a transfer efficiency of 2 % for rough-sawn wood (TNsG 2002, Part 2, p. 206)	2.99	50	Y
Infants playing on playground OIT-treated wood structures (long-term)	**Tier 1 –** no protection	149.6	50	N*
	Tier 2 – assuming a transfer efficiency of 2 % for rough-sawn wood (TNsG 2002, Part 2, p. 206)	2.99	50	Y

*See text below

The predicted concentration of OIT in treated wood is 150 ppm. This concentration is above the indicative human NOAEC for skin sensitisation of 50 ppm. However, as the OIT is bound to the matrix of the treated wood, it is considered to be unavailable for the induction of a sensitising reaction. Therefore it is concluded that there is no risk of skin sensitisation for secondary exposures.

2.2.1.3.3 Combined exposure

Not relevant.

2.2.2 ENVIRONMENTAL RISK ASSESSMENT

2.2.2.1 FATE AND DISTRIBUTION IN THE ENVIRONMENT

The available fate and behaviour data were preformed using 2-Octyl-2H-isothizaol-3-one (OIT), and all data requirements for PT8 were addressed by studies or acceptable justifications for non-submission.

OIT has been shown to degrade in both terrestrial and aquatic environments to produce a number of metabolites, The UK CA proposes that the environmental risk assessment should consider OIT for all compartments and the metabolites M1, M4, M5, M6 and M7 for any freshwater and M21 for marine compartments exposure during the use of OIT.

All calculated DT50 and Koc values which can be utilised within the risk assessment are shown below in Table 2.12 for the active substance OIT, noting where multiple DT_{50} values are available, unless stated otherwise, the UK CA have chosen the worst case DT_{50}.

Table 2.12 Calculated endpoints of the active substance, OIT

Hydrolysis DT_{50}	> 1 year
Photolysis in air DT_{50}	0.27 days
Freshwater aerobic biodegradation DT_{50}	2.3 days
Seawater aerobic biodegradation DT_{50}	5.1 days
Aerobic soil biodegradation DT_{50} (longest of 3 soils)	0.9 days
Koc (geomean of 3 soils, 1 sediment) [1]	982 l/kg
Koc (sewage sludge)	6740 l/kg
1/n (geomean of 3 soils, 1 sediment)[2]	0.8427

Fate in the aquatic compartment

OIT was found to be hydrolytically stable at pH5, 7 and 9 for more than 30 days. However it does undergo aqueous photolysis, with a photolytic half life of 15.3 days, which results in the production of 4 non-relevant metabolites , namely 2-(n-octyl)-4-thiazolin-2-one (14.1 %); a mixture of N-(n-octyl) malonamic acid and oxamic acid metabolites (12.5%) ; N-(n-octyl) acetamide (11.2 %) and RH-29187 (10.1 %).

[1] To be applied in FOCUS modelling; sorption to suspended matter and PECsediment calculations
[2] To be applied in FOCUS modelling

In simulation tests OIT was shown to biodegrade in both freshwater and seawater with DT_{50} values ranging from 1.1 – 2.7 days and 3.9 – 5.1 days respectively, with CO_2 being the major metabolite in both tests and a further three unidentified metabolites within the freshwater study.

As the aquatic biodegradation DT_{50}s are quicker than the photolysis half life, biodegradation is more likely to determine the kinetics and fate of OIT dissipation in natural waters. Additionally the quick biodegradation of OIT indicates that OIT is unlikely to accumulate in the environment.

A number of major (> 10 %) metabolite fractions were identified in the aquatic degradation studies. As discussed above, the likely high rate of microbial biodegradation in natural waters will limit the potential for significant levels of aqueous photometabolites to be formed. Therefore the aqueous photolysis metabolites will not be further considered.

A number of major metabolite fractions were identified in the freshwater biodegradation study. Three metabolites were found above 10 %, namely M1, M5 and M6 which reached maximum amounts of 22.8 %, 15.0 %, and 10.5 %, respectively and two metabolites, M4 and M7, were present at two consecutive sampling points within the low dose studies where maximum amount of 5.3 % and 7.3 % were reached. These metabolites were not identified but accounted for less than 10 % AR by the end of the high and low dose studies and were mineralised to CO_2. Within the sea water biodegradation study CO_2 and M21 were the only major metabolites identified, where M21 reached a maximum of 9.2 %.

From the sterile sea water and soil biodegradation studies, the sterile control samples behaved in a consistent manner, in that little degradation occurred and very little radioactivity was found to be bound to the solid matter (water) or formed NERs. When examined in comparison to the biodegradation study results (rapid degradation and high NERs or bound residues) it can be concluded that it is highly unlikely that OIT is contained within the bound residues at any significant concentration and the transient metabolites form the bound residues. Additionally within the studies it was observed that the bound residues continued to mineralise as the bound residues level decrease while the level of mineralization continues to increase, as such the UK CA is not concerned with any potential accumulation of the bound residues.

Overall the UK CA is of the opinion that in natural freshwater, seawater, soil and a simulated STP a fairly consistent pattern of rapid microbial degradation of OIT has been shown. The first stage in the degradation appears to be the opening of the isothiazalone ring. The major route of dissipation appears to result in significant mineralisation to CO_2, or formation of metabolite fractions that partition to the organic portion of either soil or water which then continues to mineralise over time. The UK CA proposes that the environmental risk assessment should consider OIT for all compartments and the metabolites M1, M4, M5, M6 and M7 for any freshwater and M21 for marine compartments exposure during the use of OIT.

Fate in air

Utilising Atkinson's SAR it has been calculated that OIT will rapidly transform in air, with a DT50 of 0.27 days, with vapour pressure measurements in the range of $2.64 – 3.10 \times 10^{-3}$Pa (LoEP). Therefore even if any OIT were to be emitted to the atmosphere, due to the short half life it is highly unlikely to persist within the atmosphere or be subject to long range transport.

Fate in the terrestrial compartment

In a sewage treatment plant simulation 82.9 % of the OIT was degraded and 1.1 % OIT was associated with either the sludge or the primary effluent. Soil biodegradation studies showed the DT_{50} to be 0.9 days, with CO_2 being the only major metabolite. The presence of CO_2 in the biodegradation study indicates that the isothiazole ring is cleaved. OIT was found to have a Koc value of 6740 l/kg in sludge and a soil Koc value of 982 l/kg (geometric mean).

It should be noted that while within the adsorption tests OIT was shown to strongly adsorb to soil, sediment and activated sewage sludge, and to have low mobility in soil, within the sewage simulation test, OIT was not found to be in the sludge phase. This is likely due to the rapid biodegradation of OIT in the non-sterile systems, causing very little OIT to be found associated with the sludge (≤1.1 %). Thus while OIT will bind to sludge in a non-sterile environment, the OIT will be expected to biodegrade rapidly and thus reduce the potential for sorption on to sludge.

2.2.2.2 EFFECTS ASSESSMENT

Aquatic

An assessment of the available toxicity data, identified that the most sensitive aquatic organisms to OIT are marine algae, with a NOEC of 0.68 µg l^{-1}. However, it is apparent from Table 2.13, that all the toxicity endpoints are below 200 µg l^{-1}.

Table 2.13 Summary of aquatic endpoints for OIT

Group	Timescale	Species	Endpoint	Toxicity (µg l^{-1})
Fish(freshwater)	96 hours	*Oncorhynchus. mykiss*	LC_{50}	36.0
Aquatic invertebrates (freshwater)	48 hours	*Daphnia magna*	EC_{50}	100
Aquatic invertebrates (marine)	96 hours	*Mysidopsis bahia*	EC_{50}	71.0
Aquatic invertebrates	21 days	*Daphnia. magna*	NOEC	1.6
Algae (marine)	72 hours	*Skeletonema costatum*	E_rC_{50} NOEC	**1.5** **0.68**
STW microbes	3 hours	Activated sludge	EC_{50}	30 400
Sediment dweller	Not applicable	Equilibrium partitioning method	PNEC	0.16

The PNECs highlighted in yellow were taken from the combined Document I.

Table 2.14 Summary of PNECs for OIT

Environmental compartment	PNEC
STW	304.0 µg l^{-1}
Surface water (freshwater)	0.0071 µg l^{-1}

Surface water (marine)	0.00071 µg l^{-1}
Sediment	0.16 µg kg^{-1}

Atmosphere

No studies were submitted to address this compartment. However, according to the fate and behaviour section, there is no concern that OIT will enter into the atmospheric environment.

Terrestrial

An assessment of the available toxicity data, identified that the most sensitive soil organism to OIT are soil microbes, with a NOEC of 20.0 mg kg^{-1}.

Table 2.15 Summary of soil endpoints for OIT

Group	Species	Timescale	Endpoint	Toxicity (mg kg^{-1} dw)
Soil invertebrate	*Eisenia fetida*	14 day acute	Mortality EC_{50}	866
Soil microbe	*NA*	28 days	Nitrogen transformation EC_{50}	485*
Soil microbe Key study	***NA***	**28 days**	**Nitrogen transformation NOEC**	**20***
Terrestrial plants	*Lactuca sativa*	23 days	Seedling growth NOEC	88*

NA not applicable
Values in bold denote those used to derive the PNECsoil
*Toxicity endpoints converted to allow for organic content of soil

Table 2.16 Summary of soil PNEC for OIT

Environmental compartment	PNEC
Terrestrial (soil)	400 µg kg^{-1} soil dwt 520 µg kg^{-1} soil wwt

Primary and secondary poisoning

OIT has a Log kow <4.5 and a measured BCF in fish of 92.6 L kg^{-1}. The calculated BCF for earthworms was 10.82 L kg^{-1} wet earthworm.

Table 2.17 Summary of terrestrial vertebrate endpoints for OIT

Group	Species	Timescale	Endpoint	Effect
Birds	Bobwhite quail, *Colinus virginianus*	8days	LC_{50} short-term mortality	>5000 mg OIT kg^{-1} feed
Mammals	Rat, Wistar	One generation study	NOAEL	800ppm; 43 mg OIT kg^{-1} day

The following PNECoral were taken from the combined Document I.

Table 2.18 Summary of PNECs for OIT

Environmental compartment	PNEC
Secondary poisoning: piscivorous birds	0.39 mg OIT kg food^{-1}
Secondary poisoning: piscivorous mammals	16.67 mg OIT kg food^{-1}

Bittering agent

As OIT does not contain a bittering agent, this section is not relevant.

2.2.2.3 PERSISTENT, BIOACCUMULATION AND TOXIC (PBT) ASSESSMENT

According to the TGD In line with Annex III Annex III of Regulation (EC) No 1907/2006 (REACH), the Persistent, Bioaccumulative and Toxic (PBT) assessment is considered to be different from the local and regional assessment approaches, as it seeks to protect ecosystems where risks are more difficult to estimate. Under the Biocidal Products Regulation (BPR), any active substance that is found to be either a PBT or very Persistent very Bioaccumulative (vPvB) substance shall not be Approved unless a specific derogation applies. Any active substance that now has been demonstrated to trigger any two of the P or B or T criteria must be considered as a "candidate for substitution".

Persistence

As outlined in screening criteria taken from chapter R11- PBT Assessment of the ECHA (REACH) Guidance on information requirement and chemical safety assessment, the criteria for P and vP are shown below, with a comparison for the endpoints determined for OIT, where it is illustrated that none of the criteria has been met.

Based upon the data set supplied for OIT the compound is not classified as P or vP.

P criteria	vP criteria	OIT
-$T_{1/2}$ >60 days in marine water, or -$T_{1/2}$ >40 days in fresh- or estuarine water, or -$T_{1/2}$ >180 days in marine sediment, or -$T_{1/2}$ >120 days in fresh- or estuarine sediment, or -$T_{1/2}$ >120 days in soil	$T_{1/2}$ >60 days in marine water, fresh- or estuarine water or -$T_{1/2}$ >180 days in marine, fresh- or estuarine sediment, or -$T_{1/2}$ >180 days in soil	DT_{50} seawater aerobic degradation: 5.1 days DT_{50} freshwater aerobic degradation: 2.3 days DT_{50} aerobic soil: 0.9 days DT_{50} sediment no data

Bioaccumulation

A substance is considered to have the potential to fulfil the criterion of bioaccumulation when the log K_{ow} exceeds 4.5. A log K_{ow} of 2.92 was derived for OIT, and therefore, there is no trigger for an assessment of the bioaccumulation potential of this active substance in aquatic organisms.

Toxic

A substance is considered to have the potential to fulfil the criterion of toxic when the NOEC or EC_{10} is below 0.01 mg a.s./L. There are long-term NOECs available for 3 trophic levels, with the lowest available endpoint being the 72 h NOE_rC of 0.68 µg l^{-1} for algae. Therefore, OIT is considered to fulfil the criterion of toxic.

PBT Conclusion

Although OIT fulfils the toxic criteria, it does not breach the persistent or bioaccumulation criteria therefore it can be concluded that it is not a PBT substance.

PBT assessment of relevant metabolites

During the assessment of OIT the following relevant metabolites were identified, M1, M4, M5, M6, M7 and M21. At present there is no information available other than the metabolites codes. As such following the Guidance on Information Requirements and Chemical Safety Assessment (Chapter R.11: PBT/vPvB assessment) it is concluded that '*the available information does not allow to conclude (i) or (ii). The substance may have PBT or vPvB properties. Further information for the PBT/vPvB assessment is needed. The registrant must generate relevant additional information and carry out Step 1 again, or the registrant must treat the substance as if it is a PBT or vPvB.*'

Further information on the identification and properties of the metabolites has been provided, allowing further considerations to be made. Full details are provided below, however no metabolite is to be a PBT substance.

Persistence

Both QSAR screening tests and aquatic simulation tests have been considered within the P assessment of the OIT aquatic metabolites. Using a weight of evidence approach it is concluded that all the metabolites are not 'P', This is based upon the degradation observed within the water simulation tests and the partitioning behaviour expected to occur in soil and sediment.

From the simulation tests it can be concluded that M1, M5, M6 and M21 are not persistent or very persistent in water. Metabolites M4 and M7 did not show a clear decline curve in the simulation tests and a quantitative DT50 value cannot be calculated, qualitatively observing the formation and decline of the substance it is not expected that the substances would persist in the aquatic environment.

Considering the results of the freshwater and marine simulations tests the following conclusions can be made:

Metabolite	'P' consideration
M1	Within the freshwater degradation study (Mamouni, 2007a) the calculated DT50 value ranged from 17.8 – 35.5 days (n=2) at 12°C. These values are below the freshwater P (40 days) and vP (60 days) trigger values and as such it is concluded that M1 is not P and not vP in water.
M4	Within the freshwater degradation study (Mamouni, 2007a), no DT50 value was calculated as residues were only >%AR at 2 time points. Qualitatively, observing the data set it is not expected that this substance will persist in the aquatic environment as the metabolite peaked at 5.3%AR and declined to 2.6%AR within 5 days
M5	Within the freshwater degradation study (Mamouni, 2007a) the calculated DT50 value ranged from 819.3-30.9 – 22.9 days (n=2) at 12°C. These values are below the freshwater P (40 days) and vP (60 days) trigger values and as such it is concluded that M5 is not P and not vP in water.
M6	Within the freshwater degradation study (Mamouni, 2007a) the calculated DT50 value ranged from 8.3 – 22.9 days (n=2) at 12°C. These values are below the freshwater P (40 days) and vP (60 days) trigger values and as such it is concluded that M6 is not P and not vP in water.
M7	Within the freshwater degradation study (Mamouni, 2007a), no DT50 value was calculated as residues were only >%AR at 2 time points. Qualitatively, observing the data set it is not expected that this substance will persist in the aquatic environment as the metabolite peaked at 7.3%AR and declined to 3.5%AR within 3 days.
M21	Within the seawater degradation study (Mamouni, 2007b) a DT50 value of 9.4

	days (9°C). These values are below the marine P (60 days) and vP (60 days) trigger values and as such it is concluded that M1 is not P and not vP in water.

From the simulation tests it can be concluded that M1, M5, M6 and M21 are not persistent or very persistent in water. It is expected that M4 and M7 are unlikely to persist in water.

However, it is unclear whether comparable conclusions can be made with regards to degradation in soil and sediment. QSAR BIOWIN values were calculated for all substances however no clear conclusion can be made based upon the screening information.

Considering the QSAR Koc values of the metabolites (below), it can be concluded that they are more likely to partition into water (compared to soil or sediment). Therefore, if these metabolites were to enter soil or sediment matrices it expected they would preferentially partition into the water phase where the substance will undergo biodegradation.

Considering the weight of evidence approach it is not expected that these substances would persist in the environment and are not P.

Metabolite/ Group	M1	M4 (a-b)	M5 (a-b)	M6-1a + M6-2a	M6-1b + M6-2b	M6-1 (c-g) + M6-2 (c-g)	M6-1h + M6-2h	M6-3a	M6-3b
Koc (L/Kg)	10	82.5	10	74	62.2	65.1	66.5	38.2	69.1
Metabolite/ Group	M6-3 (c-f)	M6-3g	M6-3h	M6-4a	M6-4b	M6-8 (a-b)	M7 (a+c)	M7 (b+d)	M21 (a-b)
Koc (L/Kg)	100.6	100.6	211.6	693.8	593.8	325.8	135.1	121.6	32.1

QSAR analysis (screening)

It must also be noted that it is indicated that QSAR data cannot be used to provide an overall conclusion of the persistence of a substance and instead is a useful screening tool to identify potential persist substances.

The applicant submitted QSAR analysis which calculated DT50 values making use of the programmer ChemProp. In the first instance R.11 indicates BIOWIN should be considered. The applicant has not provided further details on the validation of their selected QSAR model.

The RMS has conducted BIOWIN QSAR analysis (BIOWIN 2, 3 and 6) for the identified metabolites. Please note that M6-1 and M6-2 produce identical SMILES and as such the M6-1 values are also applicable to M6-2.

R.11 provides the following triggers for persistence:

- BIOWIN 2: Substance does not degrade fast if <0.5
- BIOWIN 3: Substance does not degrade fast if < 2.25
- BIOWIN 6: Substance does not degrade fast if <0.5

R.11 indicates the combination of results from BIOWIN 2 and 3 can be used in decision making, or the combination of results from BIOWIN 6 and 3 can be considered.

Within the results table, values greater than the trigger are green (indicating fast biodegradation), values less than the trigger value are red (indicating potentially P or vP).

At the QSAR screening step, only M5 can be stated to be 'probably not P' on the basis of all 3 BIOWIN estimates being above the relevant triggers. If only the combination of results from BIOWIN2 and BIOWIN 3 are considered all metabolites would also be predicated to be not persistent, except for M6-3b, M6-3c, M6-3d and M7b. However, in the case of M6 and M7 the equivocal information from the QSAR analysis is considered lower weight information compared with the information from the aquatic simulation studies. There is no guidance in R.11 on how to interpret results where the grouping of BIOWN results are not in agreement, however due to the existence of simulation data this is not considered further.

Metabolite	Formula	BIOWIN2	BIOWIN3	BIOWIN6
M1	$C_7H_9NO_3S$	0.7297	3.1501	0.4016
M4a	C10H16N2O5S	0.9848	3.288	0.288

M4b	C10H16N2O5S	0.9848	3.228	0.288
M5a	C8H13NO3S	0.9694	3.0604	0.5109
M5b	C8H13NO3S	0.9694	3.0604	0.5109
M6-1a	C11H19NO2S	0.7047	2.8523	0.5992
M6-1b	C11H19NO2S	0.7047	2.8523	0.3688
M6-1c	C11H19NO2S	0.7047	2.8523	0.3688
M6-1d	C11H19NO2S	0.7047	2.8523	0.3688
M6-1e	C11H19NO2S	0.9378	3.1507	0.3688
M6-1f	C11H19NO2S	0.9378	3.1507	0.3688
M6-1g	C11H19NO2S	0.9378	3.1507	0.3688
M6-1h	C11H19NO2S	0.9378	3.1507	0.3688
M6-3a	C11H17NO2S	0.9991	2.7191	0.8545
M6-3b	C11H17NO2S	0.338	2.6743	0.3659
M6-3c	C11H17NO2S	0.338	2.6743	0.3659
M6-3d	C11H17NO2S	0.338	2.6743	0.3659
M6-3e	C11H17NO2S	0.7634	2.9727	0.3659
M6-3f	C11H17NO2S	0.7634	2.9727	0.3659
M6-3g	C11H17NO2S	0.7634	2.9727	0.3659
M6-3h	C11H17NO2S	0.8354	2.9952	0.2005

M6-4a	C14H28N2O4S	0.9554	3.1317	0.2241
M6-4b	C14H28N2O4S	0.9914	3.1242	0.3154
M6-8a	C14H26N2O3S	0.9933	3.164	0.2579
M6-8b	C14H26N2O3S	0.9933	3.164	0.2579
M7a	C11H18N2O5S	0.9815	3.257	0.1394
M7b	C11H18N2O5S	0.9047	0.0449	0.3117
M7c	C11H18N2O5S	0.9815	3.257	0.1394

M7d	C11H18N2O5S	0.9047	3.0449	0.3117
M21a	$C_{11}H_{21}NO_4S$	1	3.0539	0.2482
M21 b	$C_{11}H_{21}NO_4S$	1	3.0539	0.2482

B assessment

The QSAR screening tests have been considered within the B assessment of the OIT aquatic metabolites. It is concluded that all the metabolites are not 'B', This is based upon the log Kow and predicted BCF (where relevant).

The log Kow value for all metabolites except M6-8 (a+b) are below 2, so they are below the range for the linear extrapolation of BCF presented in the guidance and clearly will not trigger B.

M6-8 (a+b) has a log Kow of 2.4907, which is below 4.5, so according to the guidance will not give a BCF high enough to trigger B, however since it is possible to calculate BCF it has been done. The BCF is 5.125. A BCF of ≥ 500 is indicative of the potential to bioaccumulate and a BCF of >2000 triggers the B classification. Since the BCF is below 2000 the metabolite is not 'B'.

T assessment

The QSAR screening tests have been considered within the T assessment of the OIT aquatic metabolites, however they are not able to give a definitive result. A conclusion on the assessment for T was not required because none of the metabolites had an acute L(E)C50 < 0.01 mg/L and the log Kow for all was <4.5.

Chronic data are not available for any of the metabolites, so the acute endpoints will be used. Acute or short-term aquatic toxicity data are considered to be screening information and may be used as an indication that the substance may fulfil the T criterion. Acute data cannot be used for concluding definitively "not T".

The lowest acute toxicity endpoint for each metabolite is shown below:

Metabolite	Group	Endpoint (mg/L)
M1	Invertebrates	4.08

M4	Algae	99.240
M5	Algae	6.502
M6-1a	Invertebrates	0.0564
M6-1e	Invertebrates	0.32
M6-1h	Algae	0.347
M6-3a	Invertebrates	0.22
M6-3e	Algae	0.444
M6-3h	Algae	0.059
M6-4a	Fish	4.23
M6-4b	Fish	8.48
M6-8 (a+b)	Fish	2.99
M7 (a+c)	Fish	68.33
M7 (b+d)	Fish	3.61
M21 (a+b)	Algae	10.514

Following the flow chart for assessing T:

Acute E(L)C 50 <0.01 mg/L	Yes for: None -> no metabolites definitively classified T No for: All -> progress to next step
Acute E(L)C 50 <0.1 mg/L	Yes for: M6-1a and M6-3h -> potentially T. Not P or B so no further assessment required. No for: All others -> progress to next step
LogKow < 4.5?	Yes for: All metabolites -> no further assessment required (T not confirmed).

2.2.2.4 POP ASSESSMENT

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

OIT has not been identified to trigger the 'P' or the 'B' criteria. Theoretically, OIT will not pose a risk for long-range transport on the basis of an estimated atmospheric half life of only 0.27 days (assuming a 12 hour day and an OH radical concentration of .5 x 10^6 cm^{-3} utilising AOPWIN (v.1.7) QSAR modelling tool)

Given the above, OIT does not meet the criteria for being a persistent organic pollutant.

2.2.2.5 EXPOSURE ASSESSMENT

The environmental exposure assessment presented within Doc IIB, Section 3.3 was based on all the relevant information available in the Organisation for Economic Co-operation and Development (OECD) series on emission scenario documents (ESD) on wood preservatives (OECD;2003) and where necessary the Technical Guidance Document (TGD; 2003).

The OECD ESD is limited to local exposure calculations for the wood preservation life cycle stages of 'product application' and 'wood in service' only. Production of the active substance (a.s.), formulation of the wood preservative product, waste treatment, recovery (out-of service use) and contamination of treatment sites have not been addressed. The local scale exposure assessments present within this document are considered to be worst-case in terms of environmental concentrations for this substance and product type. Where a particular Member State concern exists, the UK CA recommends that a detailed consideration of this should be possible at the product authorisation stage.

OIT is to be used as a wood preservative for use up to use class 2 (UC2) as defined within the OECD ESD (wood or wood-based product under cover, fully protected from the weather but where high environmental humidity can lead to occasional but not persistent wetting) within the product 'ACTICIDE® OTW 8' (8 % w/w OIT). This product is intended for use by professional users only by dipping/immersion or vacuum pressure impregnation. Automated spraying, brushing or double vacuum impregnation are not considered as part of this assessment.

Table 2.14 Table of intended uses of 'ACTICIDE® OTW 8'

MG/PT	Field of use envisaged	Concentration at which a.s. will be used
PT8	Wood preservative (UC 1 &2)	Dipping/immersion: 250 ppm OIT in treatment solution Vacuum/pressure impregnation: 150 ppm OIT in the treatment solution

For the intended use (up to UC2) of 'ACTICIDE® OTW 8' the relevant scenarios, as stated within the OECD ESD are:

- Industrial Application
  - Dipping/immersion process (Antisapstain treatment and dipping of joinery)
  - Vacuum pressure impregnation

- Industrial Storage
    - Dipping/immersion process (Antisapstain treatment and dipping of joinery)
    - Vacuum pressure impregnation

The compartments which are likely to be exposed during industrial application and subsequent storage, according to the OECD ESD, are summarised within Table 2.15.

Table 2.15 Environmental compartments expected to be exposed after use of 'ACTICIDE® OTW 8'

Life-cycle stage/ process	Compartment exposure to OIT						
	Surface water, via STP	Surface water, directly	Sediment, via partitioning	Soil, directly	Soil, indirectly	Ground water[3]	Air
Product application	Y	N	Y	N	Y	Y	Y
Storage	N	Y	Y	Y	N	Y	Y

In addition to the scenarios given in the above table, use of pre-treated timber in internal roof spaces (UC 1 & 2) is likely and may result in the direct exposure of roosting animals (e.g. birds and bats). In the UK, bats are a protected species and all products that can be used in areas where bats are known to roost (i.e. lofts and roof spaces) undergo a specific risk assessment. An assessment of the risk posed to bats by the use of the OIT in wood preservatives has not been carried out as part of this review but has been deferred to the product authorisation stage where specific Member States' concerns should be addressed.

Emissions to the environment have been considered to occur during industrial application and subsequent storage of the treated wood articles, where an application rate of 4.375×10^{-3}Kg OIT/m^3 and 0.4545g OIT/m^2 were considered within the environmental risk assessment for dipping/immersion and vacuum impregnation respectively.

Only Use class 1 and 2 are requested as part of this application, as treated timber is expected to be stored on bunded sites within the EU the UK CA is of the opinion that the scenarios outlined within the OECD ESD are not relevant. However for completeness, PEC values for OIT have been produced. On this occasion the UK CA have not calculated the subsequent freshwater metabolites as no emissions of OIT are realistically likely to occur during use, however if further use classes are sought metabolite PECs may be required to be calculated.

The calculated OIT PEC values for the main compartments of concern resulting for the above use are presented in the following tables.

[3] Indirect exposure via leaching of the substance in soil

Table 2.16 Elocal & PECstp values following industrial application of 'Acticide OTW 8'

Nomenclature	Vacuum	Dipping
$Elocal_{water}$	0.0409 kg/d	0.0131 kg/d
PEC_{stp}	3.27 µg/L	1.05 µg/L

Table 2.17 Resulting PEC_{water} (µg/L) after industrial application and storage of 'ACTICIDE® OTW 8'[4]

Application (Indirect exposure via STP)	Vacuum	Initial	0.327
	Dipping	Initial	0.105
Storage (Direct Exposure)	Vacuum	Initial	3.62
		Degraded	1.64
	Dipping	Initial	0.463
		Degraded	0.210
Industrial Processes (Combined exposure- application and storage).	Vacuum	Initial	3.95
	Dipping	Initial	0.568

Table 2.18 Resulting PEC_{sed} (mg/~~K~~kg) after industrial application and storage of 'ACTICIDE® OTW 8'

Application (Indirect exposure via STP)	Vacuum	Initial	7.23E-03
	Dipping	Initial	2.32E-03
Storage[5] (Direct Exposure)	Vacuum	Initial	8.01E-02
		Degraded	3.63E-02

[4] Degraded values do not consider adsorption to suspended sediment
[5] PECsed values for storage may be overestimated as the PECsw values were not corrected for sorption onto suspended matter.

	Dipping	Initial	1.03E-02
		Degraded	4.65E-03
Industrial Processes (Combined exposure- application and storage).	Vacuum	Initial	8.74E-02
	Dipping	Initial	1.26E-02

Table 2.19: PEC_{soil} (mg/kg wwt) values following industrial application of 'Acticide OTW 8'

(indirect exposure via STP)

Nomenclature	Vacuum	Dipping
PEC_{soil}	4.033E-05	1.292E-05
$PEC_{agr,soil}$[6]	6.721E-06	2.153E-06
$PEC_{grassland}$	2.688E-06	8.610E-07

Table 2.20 PEC_{soil} after industrial storage of 'ACTICIDE® OTW 8'

Method	Use Class	Process	Time	PEC_{Soil} (mg/kg wwt)
Vacuum Pressure	2	Application	TIME 1 (30 days)	6.31
			TIME 2 (20 years)	1.54E+03
Dipping	2	Application	TIME 1 (30 days)	6.06E-01
			TIME 2 (15 years)	1.11E+02

[6] To be considered within groundwater calculations.

Table 2.21 $PEC_{g/w}$ after industrial storage of 'ACTICIDE® OTW 8'

Method	Use Class	Process	Time	PEC_{gw} (mg/L)
Vacuum Pressure	2	Storage	TIME 1 (30 days)	0.36
			TIME 2 (2 years)	88.27
Dipping	2	Storage	TIME 1 (30 days)	0.03
			TIME 2 (15 years)	6.36

Table 2.22 $PEC_{g/w}$ after industrial application of 'ACTICIDE® OTW 8'

	Process	**Vacuum**	**Dipping**
PECgw (µg/L)	**Application**	0.00039	0.00012

It can be clearly be seen that the OIT in groundwater concentration exceeds the 0.1ug/L drinking water limit following industrial storage; normally if the first tier calculations breach the EU drinking water limit, higher tier FOCUS groundwater models are required. However on this occasion the UK CA are of the opinion that higher tier calculations will not be required in the first instance, as the only relevant OECD scenario for soil exposure (storage) is not considered to be a relevant emission pathway for the reasons explained previously. However to ensure that this emission pathway is not available, the UK CA recommend a suitable label mitigation label phrases are required, please see Doc II-C for more details.

The groundwater concentrations following industrial application do not exceed the 0.1µg/L drinking water limit; no further consideration is required in regards to industrial application.

2.2.2.6 RISK CHARACTERISATION

The applicant has stated that 'ACTICIDE® OTW 8' is to be used as a wood preservative in a closed system and therefore there will not be direct release to the environment. Only use class 1 and 2 are requested as part of this application. As treated timber is expected to be stored on bunded sites within the EU, the UK CA is of the opinion that the scenarios outlined within the

OECD ESD are not relevant. However for completeness, an aquatic risk assessment for OIT has been performed. The UK CA have not calculated the subsequent PEC for freshwater metabolites as no emissions of OIT are realistically likely to occur during use, however if further use classes are sought metabolite PECs may be required to be calculated.

2.2.2.6.1 Risk to the aquatic compartment (including sediment)

Risks to local STP

The risk quotient is less than 1 for all scenarios. It is concluded that OIT as used in 'ACTICIDE® OTW 8' is not a substance of concern to sewage treatment plants.

Risks to the aquatic compartment (surface waters)

The risk quotient ranges from 13.8 to 510, all above 1. It is concluded that OIT, as used in ACTICIDE® OTW 8' is a substance of concern to the aquatic compartment, and mitigation measures are required.

Risks to the sediment compartment

The risk quotient ranges from 0.452 to 501. Only one scenario (sediment exposure via STP following vacuum impregnation) results in a quotient less than 1. It is concluded that OIT, as used in ACTICIDE® OTW 8' is a substance of concern to the sediment compartment, and mitigation measures are required.

2.2.2.6.2 Risk to the terrestrial environment

Risks to the soil compartment

The risk quotient following industrial storage of treated wood ranges from 1.34 to 3400. It is concluded that OIT, as used in ACTICIDE® OTW 8' is a substance of concern to the terrestrial compartment, and mitigation measure are required.

It should be noted that the quotient following industrial application is less than 1 for all scenarios.

Risks to groundwater

OIT in groundwater concentration exceeds the 0.1ug/L drinking water limit following industrial storage; normally if the first tier calculations breach the EU drinking water limit, higher tier FOCUS groundwater models are required. However on this occasion the UK CA are of the opinion that higher tier calculations will not be required in the first instance, as the only relevant OECD scenario for soil exposure (storage) already requires risk mitigation measures to prevent exposure and no further consideration is required at this time.

The groundwater concentrations following industrial application do not exceed the 0.1µg/L drinking water limit; no further consideration is required in regards to industrial application.

Risks of secondary poisoning

Owing to the use of OIT in use classes 1 and 2 on bunded sites, the exposure to non-target biota is considered by the UK CA to be negligible.

2.2.3 HUMAN HEALTH AND ENVIRONMENTAL RISK ASSESSMENT SUMMARY

2.2.3.1 INDUSTRIAL USER

Human Health

Risks of systemic effects in all the primary (industrial) scenarios considered (mixing and loading, automated dipping, vacuum-pressure impregnation, cleaning dip-tank and handling treated wet wood) are acceptable even at Tier 1 (no protection = light clothing and boots).

Inhalation exposures to OIT in all industrial scenarios are very low even at Tier 1 (no protection = light clothing and boots), leading to acceptable risks of local irritative effects on the respiratory tract.

Risks of local sensitising effects on the skin and of corrosivity are considered to be acceptable for the mixing and loading scenario (coupling/uncoupling transfer lines) where the concentrate product is handled (8% OIT) only when extensive PPE (respiratory protection, gloves, coveralls and eye protection) and engineering controls (full automation) are used. For the other scenarios, where the diluted product (150-250 ppm OIT) is handled, risks of local skin sensitising effects are considered to be acceptable through the use of appropriate PPE (gloves and coveralls), minimisation of manual phases (where possible) and good hygiene practice.

Overall, safe industrial uses have been identified for OIT; however, extensive PPE (respiratory protection, gloves, coveralls and eye protection) and engineering controls (full automation) are required in the mixing and loading scenario where the concentrate product is handled (8% OIT) and appropriate PPE (gloves and coveralls) is required for the other scenarios, where the diluted product (150-250 ppm OIT) is handled.

Risks of systemic effects for all secondary exposure scenarios are acceptable. Possible risks of local irritative effects on the respiratory tract have been predicted to result from exposure to vapour released in domestic rooms. However, as the air levels calculated by the model are considered to be unrealistically high for pre-treated timber which has been stored before use, it is considered unlikely that the presence of treated timber in domestic rooms will lead to respiratory irritation.

Theoretical risks of local sensitising effects on the skin have been predicted. However, as the OIT is bound to the matrix of the treated wood, it is considered to be unavailable for the induction of a sensitising reaction. Therefore it is concluded that there is no unacceptable risk of skin sensitisation for secondary exposures.

Environment

In all environment exposure scenarios, aquatic compartment, atmosphere, terrestrial compartment and secondary poisoning, and based on negligible exposure, the UK CA considers that risks are acceptable.

2.2.4 ASSESSMENT OF ENDOCRINE DISRUPTOR PROPERTIES

OIT is not classified for carcinogenicity or reproductive toxicity. Therefore, OIT does not meet the interim criteria for endocrine disruptors. In addition, there is no evidence in the available toxicity studies of effects on the endocrine system.

2.3 OVERALL CONCLUSIONS

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

This evaluation covers the use of OIT in product type 8. OIT belongs to a group of chemicals known as the isothiazolones. OIT acts via a two step mechanism involving rapid inhibition (minutes) of growth and metabolism, followed by irreversible cell damage resulting in loss of viability (hours). Specifications for the reference source are established.

The physico-chemical properties of the active substance and biocidal product have been evaluated and are deemed acceptable for the appropriate use, storage and transportation of the active substance and representative biocidal product.

An acceptable analytical method is available for the active substance as manufactured and for the relevant and significant impurities. A validated analytical method is available for the determination of OIT in soil and water. No analytical methods were required for air, body fluids and tissues, or residues in food/feeding stuffs.

There is no harmonised classification for OIT. The evaluating Competent Authority (eCA) intends to submit the following proposal on harmonised classification to ECHA during 2015:

The classification and labelling for OIT according to Regulation (EC) No 1272/2008 (CLP Regulation) is:

Classification according to Regulation (EC) No 1272/2008	
Hazard Class and Category Codes	Acute Tox. 3; Acute Tox. 2; Skin Corr. 1B; STOT SE 3; Skin Sens.1A; Aquatic acute 1; Aquatic chronic 1;
Labelling	
Pictograms	GHS09
Signal Word	Danger

Hazard Statement Codes	H301 Toxic if swallowed H311 Toxic in contact with skin H331 Toxic if inhaled H314 Causes severe skin burns & eye damage H335 May cause respiratory irritation H317 May cause an allergic skin reaction (specific concentration limit of C ≥ 0.005%) H400 Very toxic to aquatic life H410 Very toxic to aquatic life with long lasting effects

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

OIT is intended to be used by professional operators in industrial situations (UCs 1&2) as a fungicide to protect freshly sawn timber from blue staining fungi and surface mould growth during storage and processing. The data on OIT has demonstrated sufficient efficacy against blue stain fungi and moulds. The UK CA therefore considers that the data on the active substance are sufficient for active substance approval to be recommended. The UK CA has accepted the Applicant's reasoned case that resistance to OIT is not a significant issue.

c) Risk characterisation for human health

Summary table: scenarios			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure** **Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
1.	Mixing & loading	Primary Dilution of concentrated product (8% OIT) in a fully automated dosing system – exposure can arise from coupling/uncoupling transfer lines	Industrial
2.	Automated dipping	Primary Dipping of timber in 0.025% OIT solution through fully automated process – exposure can arise only when tension straps fail and operator manually handles treated wet wood.	Industrial
3.	Vacuum-pressure impregnation	Primary Loading of untreated wood and removal of treated (0.015% OIT) wet wood.	Industrial
4.	Cleaning dip tank	Primary Cleaning dip tank (0.025% OIT)	Industrial
5.	Handling treated wet wood	Primary Handling occasionally treated (0.025% OIT) wet wood	Industrial
6.	Professional sanding OIT-treated wood	Secondary Sanding of OIT-treated wood in a professional setting.	Professional

7.	Non-professional sanding OIT-treated wood	Secondary Sanding of OIT-treated wood in a professional setting.	Non-professional
8.	Infants chewing OIT-treated wood	Secondary Infants chewing OIT-treated wood off-cut	General public
9.	Volatilised residues from indoor OIT-treated timber	Secondary Inhalation exposure to volatilised residues from indoor OIT-treated timber	General public
10.	Infants playing on OIT-treated wood structures	Secondary Infants playing on OIT-treated wood structures	General public

Conclusion of risk characterisation for **industrial user**

Systemic effects

Scenario	**Relevant reference value**[7]	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
1.	0.056 mg/kg bw/d (long-term AEL)	Negligible	Negligible	Yes
2.	0.056 mg/kg bw/d	0.0161	29%	Yes
3.	0.056 mg/kg bw/d	0.029	52%	Yes
4.	0.056 mg/kg bw/d	0.0161	29%	Yes
5.	0.056 mg/kg bw/d	0.0161	29%	Yes

[7] Indicate which reference value is used (e.g. $AEL_{short\text{-}term}$, $AEL_{medium\text{-}term}$) and the value.

Local respiratory effects

Scenario	Relevant reference value[8]	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
1.	0.04 mg/m^3 (long-term inhalation AEC)	Negligible	Negligible	Yes
2.	0.04 mg/m^3	Negligible	Negligible	Yes
3.	0.04 mg/m^3	0.0003	0.75%	Yes
4.	0.04 mg/m^3	Negligible	Negligible	Yes
5.	0.04 mg/m^3	Negligible	Negligible	Yes

Local dermal effects

Risks of local sensitising effects on the skin and of corrosivity are considered to be acceptable for the mixing and loading scenario (coupling/uncoupling transfer lines; scenario 1) where the concentrate product is handled (8% OIT) only when extensive PPE (respiratory protection, gloves, coveralls and eye protection) and engineering controls (full automation) are used. For the other scenarios (scenarios 2-5), where the diluted product (150-250 ppm OIT) is handled, risks of local skin sensitising effects are considered to be acceptable through the use of appropriate PPE (gloves and coveralls), minimisation of manual phases (where possible) and good hygiene practice.

Conclusion of risk characterisation for **indirect exposure**

Systemic effects

Scenario	Relevant reference value[2]	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
6.	0.056 mg/kg bw/d (long-term AEL)	0.00076	1.3%	Yes
7.	0.11 mg/kg bw/d (short-term AEL)	0.00069	0.6%	Yes

[8] Indicate which reference value is used (e.g. $AEL_{short\text{-}term}$, $AEL_{medium\text{-}term}$) and the value.

8.	0.11 mg/kg bw/d (short-term AEL)	0.0084	8%	Yes
9.	0.056 mg/kg bw/d (long-term AEL)	0.0371	66%	Yes – ventilated room
10.	0.056 mg/kg bw/d (long-term AEL)	0.0065	12%	Yes

Local respiratory effects

Scenario	**Relevant reference value[2]**	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
6.	0.04 mg/m^3 (long-term inhalation AEC)	0.00075	1.9%	Yes
7.	0.08 mg/m^3 (short-term inhalation AEC)	0.00075	0.9%	Yes
8.	0.08 mg/m^3 (short-term inhalation AEC)	Not applicable	Negligible	Yes
9. Constant rate model	0.04 mg/m^3 (long-term inhalation AEC)	0.046	115%	No*
9. Evaporation model	0.08 mg/m^3 (short-term inhalation AEC)	0.244	305%	No**
10.	0.04 mg/m^3 (long-term inhalation AEC)	Not applicable	Negligible	Yes

*Although the Tier 2 calculation of exposure to volatilised residues indoors using the constant rate model predicts unacceptable exposure levels for local effects, it is noted that this calculation is based on the unrealistic worst case scenario that the active substance will be released over a year and that an individual will be exposed for 24 hours/day, every day throughout this period.

** The Tier 2 calculation of exposure to volatilised residues indoors using the evaporation model is based on a high initial release rate resulting in a high mean event concentration of 0.23 mg/m^3. Although this calculation predicts an unacceptable exposure level for local effects, it is noted that the emission from solid matrices like wood is not perfectly described by the ConsExpo tool which overestimates the diffusion of the active substance through the wood. It is also noted that this calculation predicts that air levels will drop to zero after approximately 1.5 months meaning

that the substance is totally depleted from the wood over this short period, which would seem unlikely in terms of product efficacy. In reality, the preservative is not applied on site but as a pre-treatment and, following application, the treated timber is dried and stored at the treatment site before being transported to a builder's merchant and stored again until purchase by the end user. The calculated initial peak in the emission from newly treated timber is therefore unlikely to result in the air concentrations predicted by the model when installed in domestic rooms.

Local dermal effects

In the secondary exposure scenarios where dermal contact is possible (non-professional sanding treated wood and infants playing on OIT-treated structures), theoretical risks of local sensitising effects on the skin have been predicted on the basis of a semi-quantitative assessment with the NOAEC of 50 ppm for skin sensitisation. However, as the OIT is bound to the matrix of the treated wood, it is considered to be unavailable for the induction of a sensitising reaction. A Tier 2 assessment assuming a transfer efficiency of 2 % for rough-sawn wood (TNsG 2002, Part 2, p. 206) predicts acceptable exposure levels. Therefore it is concluded that there is no unacceptable risk of skin sensitisation for secondary exposures.

Overall conclusion on human health risk characterization

Risks of systemic effects in all the primary (industrial) scenarios considered (mixing and loading, automated dipping, vacuum-pressure impregnation, cleaning dip-tank and handling treated wet wood) are acceptable even at Tier 1.

Inhalation exposures to OIT in all industrial scenarios are very low even at Tier 1, leading to acceptable risks of local irritative effects on the respiratory tract.

Risks of local sensitising effects on the skin and of corrosivity are considered to be acceptable for the mixing and loading scenario (coupling/uncoupling transfer lines) where the concentrate product is handled (8% OIT) only when extensive PPE (respiratory protection, gloves, coveralls and eye protection) and engineering controls (full automation) are used. For the other scenarios, where the diluted product (150-250 ppm OIT) is handled, risks of local skin sensitising effects are considered to be acceptable through the use of appropriate PPE (gloves and coveralls), minimisation of manual phases (where possible) and good hygiene practice.

Overall, safe industrial uses have been identified for OIT; however, extensive PPE (respiratory protection, gloves, coveralls and eye protection) and engineering controls (full automation) are required in the mixing and loading scenario where the concentrate product is handled (8% OIT) and appropriate PPE (gloves and coveralls) is required for the other scenarios, where the diluted product (150-250 ppm OIT) is handled.

Risks of systemic effects for all secondary exposure scenarios are acceptable. Possible risks of local irritative effects on the respiratory tract have been predicted to result from exposure to vapour released in domestic rooms. However, as the air levels calculated by the model are considered to be unrealistically high for pre-treated timber which has been stored before use, it is considered unlikely that the presence of treated timber in domestic rooms will lead to respiratory irritation.

d) Risk characterisation for environment

The table below summarises the exposure scenarios assessed:

Summary table: environment scenarios	
Scenario	**Description of scenario including environmental compartments**
Product Application	Surface water through losses to STP
Product Application	Sediment through losses to STP
Product Application	Atmosphere through losses to STP
Storage	Surface water (direct)
Storage	Sediment (direct)
Storage	Soil (direct)
Storage	Groundwater (direct)
Storage	Atmosphere (direct)

The scenario used for the environmental risk assessment (based upon relevant Emission Scenarios) is for use up to use class 2 (UC2) as defined within the OECD ESD (wood or wood-based product under cover, fully protected from the weather but where high environmental humidity can lead to occasional but not persistent wetting). It should be noted that within the EU it is expected that treated timber will be stored on a bunded sites as such the scenarios outlined within the OECD ESD are not considered to be realistic of EU conditions, however for completeness, a risk assessment was produced following the stated scenarios.

Application of the representative product is made only by professional users where application is made by dipping/immersion (250ppm) or vacuum pressure impregnation (150ppm) methods. The risk assessment assumed an application rate of 4.375×10^{-3} Kg OIT/m^3 and 0.4545g OIT/m^2 for dipping/immersion and vacuum-pressure impregnation respectively. As no acceptable wood leaching study was submitted leaching was set to a default 100%, this is recognised to be a highly unrealistic value, however there is no alternative default value.

However, it must be noted that any future increase in application or use pattern of OIT based products would likely result in significantly increased emissions to environmental compartments and these should be assessed for risk by MS at product authorisation. Furthermore, additional supporting data may also be required on the active substances in order to support these new assessments.

e) Overall conclusion evaluation including need for risk management measures

Risks of systemic effects in all the primary (industrial) scenarios considered (mixing and loading, automated dipping, vacuum-pressure impregnation, cleaning dip-tank and handling treated wet wood) are acceptable even at Tier 1 (no protection = light clothing and boots).

Inhalation exposures to OIT in all industrial scenarios are very low even at Tier 1 (no protection = light clothing and boots), leading to acceptable risks of local irritative effects on the respiratory tract.

Risks of local sensitising effects on the skin and of corrosivity are considered to be acceptable for the mixing and loading scenario (coupling/uncoupling transfer lines) where the concentrate product is handled (8% OIT) only when extensive PPE (respiratory protection, gloves, coveralls and eye protection) and engineering controls (full automation) are used. For the other scenarios, where the diluted product (150-250 ppm OIT) is handled, risks of local skin sensitising effects are considered to be acceptable through the use of appropriate PPE (gloves and coveralls), minimisation of manual phases (where possible) and good hygiene practice.

Overall, safe industrial uses have been identified for OIT; however, extensive PPE (respiratory protection, gloves, coveralls and eye protection) and engineering controls (full automation) are required in the mixing and loading scenario where the concentrate product is handled (8% OIT) and appropriate PPE (gloves and coveralls) is required for the other scenarios, where the diluted product (150-250 ppm OIT) is handled.

Risks of systemic effects and local irritative effects on the respiratory tract for all secondary exposure scenarios are acceptable. Theoretical risks of local sensitising effects on the skin have been predicted. However, as the OIT is bound to the matrix of the treated wood, it is considered to be unavailable for the induction of a sensitising reaction. Therefore it is concluded that there is no unacceptable risk of skin sensitisation for secondary exposures.

The UK CA proposes that OIT products should only be permitted for industrial use at industrial wood treatment sites that can comply with the following requirements to prevent losses of treatment solution and leachate to the aquatic and terrestrial environment.

- Application processes must be carried out within a contained area;
    - Situated on impermeable hard standing,
    - Within bunding to prevent run-off and
    - A recovery system in place (e.g. sump)
- Storage of treated wood must be either;
    - Undercover with a recovery system in place (e.g. sump) or
    - On impermeable hard standing and bunded to prevent run-off with a recovery system in place (e.g. sump)

The UK CA considers that these measures are reasonable requirements for all industrial wood treatment sites to prevent unnecessary contamination of the environment and is common to be available practice (BAP) throughout much of the existing industry in the UK.

f) Exclusion criteria and candidates for substitution criteria of new BPR (EU 528/2012)

Article 5 (exclusion criteria) of the Biocidal Products Regulation (BPR) states that an active substance cannot be approved if it: (1) is classified or meets the criteria for classification as CMR 1A or 1B in accordance with the CLP Regulations; (2) is considered to have endocrine-

disrupting properties; (3) or meets the criteria for PBT or vPvB according to Annex XIII to the REACH Regulation.

Article 10 (candidate for substitution criteria) of the new BPR states that an active substance should be considered a candidate for substitution if:

(a) it meets one of the exclusion criteria;
(b) it is classified or meets the criteria for classification as a respiratory sensitiser (Resp Sens 1) under the CLP Regulation;
(c) its AEL and/or AEC values are significantly lower than those of the majority of approved active substances for the same product type and use scenario;
(d) it meets two of the criteria for PBT according to Annex XIII to the REACH Regulation;
(e) there are reasons for concern linked to the nature of the critical effects which in combination with the use patterns and amount used could still cause concern, such as high potential of risk to groundwater;
(f) it contains a significant proportion of non-active isomers or impurities.

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

Property		**Classification**
CMR properties	Carcinogenicity (C)	Not C
	Mutagenicity (M)	Not M
	Toxic for reproduction (R)	Not R
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	Not P and not vP
	Bioaccumulative (B) or very Bioaccumulative (vB)	Not B and not vB
	Toxic (T)	T
Respiratory sensitisation	No classification required	
Endocrine disrupting properties	There is no evidence in the available toxicity studies of effects on the endocrine system.	
Concerns linked to critical effects	OIT does not fulfil criterion (e) of Article 10(1)	
Proportion of non-active isomers or impurities	As the proportion of impurities is below 20% OIT does not fulfil criterion (f) of Article 10(1)	

Consequently, the following is concluded:

OIT does not meet the exclusion criteria laid down in Article 5 of Regulation (EU) No 528/2012.

OIT does not meet the conditions laid down in Article 10 of Regulation (EU) No 528/2012, and is therefore not considered as a candidate for substitution. The exclusion and substitution criteria were assessed in line with the "Note on the principles for taking decisions on the approval of active substances under the BPR" agreed at the 54th meeting of the representatives of Member States Competent Authorities for the implementation of Regulation 528/2012 concerning the

making available on the market and use of biocidal products[9]. This implies that the assessment of the exclusion criteria is based on Article 5(1) and the assessment of substitution criteria is based on Article 10(1)(a, b and d).

g) Persistent organic pollutant (POP) criteria

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

OIT has not been identified to trigger the 'P' or the 'B' criteria. Theoretically, OIT will not pose a possible risk for long-range transport on the basis of an estimated atmospheric half life of only 0.27 days (assuming a 12 hour day and an OH radical concentration of .5 x 10^6 cm^{-3} utilising AOPWIN (v.1.7) QSAR modelling tool)

Given the above, OIT does not meet the criteria for being a persistent organic pollutant.

2.4 LIST OF ENDPOINTS

In order to facilitate the work of Member States in granting or reviewing authorisations, the most important endpoints, as identified during the evaluation process, are listed in Appendix I.

2.5 PROPOSAL ON THE APPLICATION FOR APPROVAL OF OIT IN PT 8

In view of the conclusions of the evaluation, it is proposed that OIT shall be approved and be included in the Union list of approved active substances, subject to the following specific conditions:

- Products may be used where wood (or wood based product) is under cover, fully protected from the weather but where high environmental humidity can lead to occasional but not persistent wetting, (i.e. up to use class 2).
- All industrial treatment processes (application and storage) should be contained with a recovery process by being either under cover or use impermeable hard standing and restrict any direct losses to drains where practicable.

2.6 ELEMENTS TO BE TAKEN INTO ACCOUNT BY MEMBER STATES WHEN AUTHORISING PRODUCTS

Further efficacy data to support the label claims and proposed application rates will be required at product authorisation.

[9] See document: Note on the principles for taking decisions on the approval of active substances under the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/c41b4ad4-356c-4852-9512-62e72cc919df/CA-March14-Doc.4.1%20-%20Final%20-%20Principles%20for%20substance%20approval.doc)

In accordance with HEEG Opinion 18 of MOTA Version 6, 'Exposure assessment for professional operators undertaking industrial treatment of wood by fully automated dipping' endorsed at TM III 2013, the following label restriction for fully automated dipping applies:

'ACTICIDE® OTW 8 *must only be used in fully automated dipping processes where all steps in the treatment and drying process are mechanised and no manual handling takes place including when the treated articles are transported through the dip tank to the draining/drying and storage areas (if not already surface dry before moving to storage). Where appropriate, the wooden articles to be treated must be fully secured (e.g. via tension belts or clamping devices) prior to treatment and during the dipping process, and must not be manually handled until after the treated articles are surface dry.'*

Application rates greater than that presented within the environmental risk assessment will require further assessment of environmental risk.

Losses during industrial application by the dipping and vacuum impregnation process, as well as during tank cleaning, must be contained (no drain connection to storm drains or STPs) and recycled; or collected and treated as waste in accordance with the national regulations of the Member State authorising individual products;

The need to address any specific national conditions and/or undertake regional assessments should be considered, as only local environmental risk assessments have been carried out in this evaluation.

The need for a risk assessment for bats should be determined at a national level.

Wood treated with OIT-containing biocidal product is not intended for and should contain label restrictions against use in areas where it could come into contact with food e.g. food for human consumption is prepared, consumed or stored, or where the feedingstuff for livestock is prepared, consumed or stored.

2.7 REQUIREMENT FOR FURTHER INFORMATION

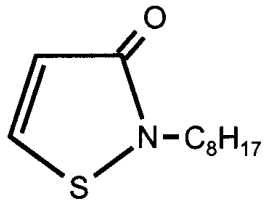
Sufficient data have been provided to verify the conclusions on the active substance, permitting the proposal for the approval of OIT in PT8.

Appendix I: List of endpoints

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

Active substance (ISO Common Name)	Octhilinon (OIT)
Product-type	Product type 8
Applicant	Thor GmbH

Identity

Chemical name (IUPAC)	2-Octyl-isothiazol-3(2H)-one
Chemical name (CA)	2-(n-Octyl)-2H-isothiazol-3-one
CAS No	26530-20-1
EC No	247-761-7
Other substance No.	-
Minimum purity of the active substance as manufactured (g/kg or g/l)	960 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	See confidential annex No relevant impurities
Molecular formula	$C_{11}H_{19}NOS$
Molecular mass	*213.3 g/mol*
Structural formula	 2-n-Octyl-2H-isothiazol-3-one

Physical and chemical properties

Melting point (state purity)	21.4 °C (Purity 96.8 %)
Boiling point (state purity)	no boiling point/range could be observed (1009 hPa; Purity >99 %).
Temperature of decomposition	267°C
Appearance (state purity)	yellow liquid with mild odour (not stated)
Relative density (state purity)	1.040 (> 99%)
Surface tension	35.97 (mN/m at 20.1°C, 90 % saturation concentration)
Vapour pressure (in Pa, state temperature)	3.1 x10^{-3} Pa (20°C ; Purity >99%) 6.1 x 10^{-3} Pa (25° C ; Purity >99%)
Henry's law constant (Pa m^3 mol^{-1})	3.14 x 10^{-3} Pa m^3/mol
Solubility in water (g/l or mg/l, state temperature)	pH 5 0.456 g/L at 10°C 0.406 g/L at 20°C 0.394 g/L at 30°C
	pH 7 0.451 g/L at 10°C 0.406 g/L at 20°C 0.395 g/L at 30°C
	pH 9 0.483 g/L at 10°C 0.433 g/L at 20°C 0.448 g/L at 30°C
Solubility in organic solvents (in g/l or mg/l, state temperature)	*In acetone* >491.59 g/L (at 10°C) > 498.40 g/L (at 20°C)
	In n-octanol >540.81g/L (at10°C) > 524.77 g/L (at 20°C)
Stability in organic solvents used in biocidal products including relevant breakdown products	There are no solvents in the technical material as manufactured.

Partition coefficient (log P_{OW}) (state temperature)	>3.1 (20°C) Based on a solubility of OIT in n-octanol of >524.8 g/L (at 20°C) and a solubility of OIT in water of 0.406 g/L (at 20°C).
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH5: >1 year
	pH7: >1 year
	pH9: >1 year
Dissociation constant	pKa = 5.2 to 6.0 x10^{-4} mol/L in diluted aqueous solution
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Absorption max. at 280 nm Extinction coefficient (280 nm): log ε = 3.92 The absorption at different pH has not been assessed.
Photostability (DT_{50}) (aqueous, sunlight, state pH)	Photolysis in air DT_{50}: 0.27 days (calculated) Aqueous photolysis DT_{50} 3.7 days (50°N; pH7) 5.1 days (50°N; pH8)
Quantum yield of direct phototransformation in water at Σ > 290 nm	Not calculated, and not required to be submitted
Flammability	Not flammable Auto ignition temperature: 330°C
Explosive properties	Not explosive

Classification and proposed labelling

with regard to physical/chemical data	None
with regard to toxicological data	**Proposed classification according to Regulation 1272/2008** Acute Tox. 3; H301 Acute Tox. 3; H311 Acute Tox. 3; H331 Skin Corr. 1B; H314 STOT SE 3; H335 Skin Sens.1A; H317 Specific concentration limit: Skin Sens.1A, C ≥ 0.005 %
with regard to fate and behaviour data	None
with regard to ecotoxicological data	**Proposed classification according to Regulation 1272/2008** Aquatic acute 1; H400 Aquatic chronic 1; H410

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	Quantitative NMR (The method is sufficient to support the batch analysis data, a more commonly available technique may be required for monitoring purposes – HPLC method is available for the product which is normally monitored due to technical material being difficult to purchase)
Impurities in technical active substance (principle of method)	See confidential appendix No relevant impurities

Analytical methods for residues

Soil (principle of method and LOQ)	Residue definition: OIT only LC-MS, single ion monitoring (0.01 mg/kg) A confirmatory method is required.
Air (principle of method and LOQ)	A method is not required as it is not sprayed and VP is less than 0.01 Pa
Water (principle of method and LOQ)	Residue definition: OIT only LC-MS, single ion monitoring (0.1 µg/L – surface water) A confirmatory method is required.
Body fluids and tissues (principle of method and LOQ)	Although OIT is classified as toxic a method for body fluids and tissues is not required as OIT dissipates rapidly in the body, OIT does not cause systemic toxicity and the metabolites observed are not regarded as of a concern.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	A method is not required for the intended use.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	A method is not required for the intended use.

Chapter 3: Impact on Human Health – agreed at WGII 2014

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	70%
Rate and extent of dermal absorption:	40% for OIT in aqueous solution at low concentration [0.02 - 0.1%]; 75% for concentrations 0.1 – 5%; 100% at corrosive concentrations (>5% OIT)
Rate and extent of inhalative absorption:	Default value of 100% proposed in absence of specific toxicokinetic data
Distribution:	Widespread
Potential for accumulation:	Low
Rate and extent of excretion:	Almost complete elimination at 96 h
Toxicologically significant metabolite(s)	None

Acute toxicity

Rat LD_{50} oral	125 mg/kg, Acute Tox. 3; H301
Rat LD_{50} dermal	311 mg/kg, Acute Tox. 3; H311
Rat LC_{50} inhalation	0.27 mg/l, 4 h, Acute Tox.3; H331 May cause respiratory irritation H335
Skin irritation	Skin Corr. 1; H314
Eye irritation	Skin Corr. 1; H314
Skin sensitization (test method used and result)	Buehler, positive, Skin Sens.1A LLNA, positive. GPMT, positive; human data; Skin Sens.1A; H317

Repeated dose toxicity

Species/ target / critical effect	Local irritation of stomach (rat/mouse), skin (rat/rabbit), respiratory tract (rat)
Lowest relevant oral NOAEL / LOAEL	NOAEC 500 ppm in diet, 49 d and 18 mo studies in mice
Lowest relevant dermal NOAEL / LOAEL	NOAEC 0.3 % (0.02 mg/cm^2), 3 mo study in rat = 14.9 mg/kg bw/d systemic
Lowest relevant inhalation NOAEL / LOAEL	NOAEC 0.64 mg/m^3, 3 mo (6 h/d, 5 d/w) study in rat

Genotoxicity	*In vitro*: negative Ames and MCGM tests, positive cytogenetics, negative cytogenetics *In vivo*: negative cytogenetics, micronucleus, negative UDS assay

	Overall, OIT is not considered to be an *in vivo* systemic genotoxin.

Carcinogenicity

Species/type of tumour	Mice: no tumour response
Lowest dose with tumours	Not relevant

Reproductive toxicity

Species/ Reproduction target / critical effect	Rat: no evidence of adverse effects on fertility or reproductive performance
Lowest relevant reproductive NOAEL / LOAEL	NOAEL 43 mg/kg/day (the highest dose tested in rat 2-generation study)
Species/Developmental target / critical effect	Rabbit: abortions, reduced foetal weight, considered to be secondary to maternal toxicity
Developmental toxicity	
Lowest relevant developmental NOAEL / LOAEL	NOAEL 20 mg/kg/day (rabbit)

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	None
Lowest relevant neurotoxicity NOAEL / LOAEL.	Not relevant

Other toxicological studies

.....	Repeat insult patch tests in human volunteers provide evidence of skin sensitisation at induction/challenge concentrations as low as 100 ppm

Medical data

.....	Skin sensitisation in humans

Summary (all agreed at WGII 2014)	Value	Study	Safety factor
Short, medium and long term $AEC_{(oral/dermal)}$	None derived ; however an indicative dermal NOAEC of 50 ppm set for skin sensitisation		
Short and medium term $AEC_{(inhalation)}$	0.08 mg/m^3	3 mo (6 h/d, 5	8

Long term $AEC_{(inhalation)}$	0.04 mg/m^3	d/w) inhalation study in rats	16
AELs	0.11 mg/kg bw/d (short-term)	90-d dermal study in rats (NOAEL = 15 mg/kg bw/d)	100 & 75% dermal abs
	0.11 mg/kg bw/d (medium-term)	90-d dermal study in rats (NOAEL = 15 mg/kg bw/d)	100 & 75% dermal abs
	0.056 mg/kg bw/d (long-term)	90-d dermal study in rats (NOAEL = 15 mg/kg bw/d)	200 & 75% dermal abs

Acceptable exposure scenarios (including method of calculation)

Professional users	Safe industrial uses have been identified for OIT; however, extensive PPE (respiratory protection, gloves, coveralls and eye protection) and engineering controls (full automation) are required in the mixing and loading scenario where the concentrate product is handled (8% OIT) and appropriate PPE (gloves and coveralls) is required for the other scenarios, where the diluted product (150-250 ppm OIT) is handled.
Production of active substance:	Not assessed under BPR
Formulation of biocidal product	Not assessed under BPR
Secondary exposure	Risks of systemic effects and local irritative effects on the respiratory tract for all secondary exposure scenarios are acceptable. Theoretical risks of local sensitising effects on the skin have been predicted. However, as the OIT is bound to the matrix of the treated wood, it is considered to be unavailable for the induction of a sensitising reaction. Therefore it is concluded that there is no unacceptable risk of skin sensitisation for secondary exposures.
Non-professional users	Not assessed as representative product is only for industrial use
Indirect exposure as a result of use	See secondary exposure

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water	
Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH5: > 1 year at 12°C
	pH7: > 1 year at 12°C
	pH9: > 1 year at 12°C
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Photolysis in air DT_{50}: 0.27 days (calculated) Aqueous photolysis DT_{50}: 3.7 days (50°N; pH7) 5.1 days (50°N; pH8) Metabolites: N-(N-octyl) acetamide (M8) (23.3% 4 DAT) N-(N-octyl) ethyl amine (M3) (16.2% at study termination) M7 (55.1% at study termination) While several metabolites were detected, freshwater biodegradation is considered a more relevant route of degradation, therefore no photolysis metabolites are considered within the risk assessment.
Readily biodegradable (yes/no)	No (No acceptable study submitted)
Biodegradation in freshwater	DT_{50}: 1.1 days - 2.3 days (n=2) Relevant Metabolites (maximum occurrence): M1 (22.8% ;7DAT), M4 (5.3%; 5DAT), M5(15.0%; 5DAT), M6 (10.5%; 3DAT) and M7(7.3%; 7DAT)
Biodegradation in seawater	DT_{50} (9°C): 3.9 days – 5.1 days (n=2) Relevant Metabolites: M21 (9.2%; 3DAT)
Biodegradation in a STP	82.9% biodegradation during the plateau phase No analysis was carried out to quantify or identify metabolites.
Distribution in water / sediment systems (active substance)	No data submitted and not required.
Distribution in water / sediment systems (metabolites)	No data submitted and not required.
Mineralization	No data submitted and not required.
Non-extractable residues	No data submitted and not required.

Route and rate of degradation in soil	
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50} (lab) (12°C aerobic): 0.7 days (normalised from 20°C study
	DT_{50} (lab) (6°C aerobic): 0.9 days (normalised from 6°C study)

Mineralization (aerobic)	$^{14}CO_2$ reached maximum levels of: Soil I: 47.6 % (Study termination) Soil II: 43.8%: (Study termination) Soil III: 42.4%: (Study termination) Soil I (6°C study): 33.7%: (Study termination)
Non-extractable residues	NER formed rapidly (c. 20% within a few hours), peaking at 48 to 51% after 7 to 14 days, declining slightly to c. 36 to 39% by 100 days. 2% NER was observed within the sterile soil (12 DAT), suggesting that the majority of NER observed within the non-sterile soil was likely to be minor metabolites formed following rapid microbial degradation of OIT and then released slowly over time, rather than unchanged parent material. Further characterisation of the NER residue showed 75% of the radioactivity was associated with the humin and humic acid fractions rather than fluvic acid, which confirms that microbial degradation is the most important route of degradation for OIT.
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	None
Field studies (state location, range or median with number of measurements)	No data submitted and not required
Anaerobic degradation	No data submitted and not required
Soil photolysis	No data submitted and not required
Non-extractable residues	No data submitted and not required
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	No data submitted and not required
Soil accumulation and plateau concentration	No data submitted and not required
Laboratory studies (range or median, with number of measurements, with regression coefficient)	No data submitted and not required

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	K_a (geometric mean of 3 soils, 1 sediment):4.60541 K_f (1 sewage sludge): 2130 K_aOC (geometric mean of 3 soils, 1sediment): 982 l/kg K_aOC (arithmetic mean of 3 soils, 1sediment): 1022.751 l/kg $K_f$oc (1 sewage sludge): 6740 l/kg No

Fate and behaviour in air

Direct photolysis in air	No data submitted and not required.
Quantum yield of direct photolysis	No data submitted and not required.
Photo-oxidative degradation in air	Atkinson calculation method using AOPWIN, vers. 1.88. Atmospheric (12 hour day) DT_{50} = 0.27 days in the presence of hydroxyl radicals (mean OH concentration of OH radicals cm^{-3})
Volatilization	Vapour pressure: 7Pa [25 °C] Henrys Law Constant: Pa m^3/mol

Monitoring data, if available	
Soil (indicate location and type of study)	No data submitted and not required
Surface water (indicate location and type of study)	
Ground water (indicate location and type of study)	
Air (indicate location and type of study)	

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	96 h	LC_{50}	36 µg/l
Invertebrates			
Daphnia magna	21 d	NOEC	1.6 µg/l
M. bahia	96 h	EC_{50}	13 µg/l
Algae			
Skeletonema costatum	72 h	NOEC	0.68 µg/l
	72 h	E_rC_{50}	1.5 µg/l
Microorganisms			
Activated sewage sludge respiration inhibition	3 h	NOEC	30.4 mg/l
Aquatic plants			
Lemna gibba	7 d	NOEC	8.7 µg/l
	7 d	EC_{50}	620 µg/l

Effects on earthworms or other soil non-target organisms ACTIVE: OIT

Acute toxicity to *Eisenia fetida*	866 mg OIT kg^{-1} soil dwt
Terrestrial plants	88 mg OIT kg^{-1} soil dwt

Effects on soil micro-organisms

Nitrogen transformation	20 mg OIT kg^{-1} soil dwt

Effects on terrestrial vertebrates

Acute toxicity to mammals	800 ppm
Acute toxicity to birds	384 mg OIT kg^{-1} feed

Dietary toxicity to birds	>5000 mg OIT kg^{-1} feed
Reproductive toxicity to birds	Not available

Effects on honeybees

Acute oral toxicity Acute contact toxicity	Not available

Effects on other beneficial arthropods

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

Bioconcentration

Bioconcentration factor (BCF)	92.6 L kg^{-1} (5 % lipid)
Depuration time(DT_{50}) (DT_{90}) Level of metabolites (%) in organisms accounting for > 10 % of residues	1.97 days Not available 5%

Chapter 6: Other End Points

None.

Appendix II: List of Intended Uses

OIT has been evaluated for its intended use as a wood preservative (PT 8); data were provided and accepted in support of this intended use.

The product is intended for use by professional operators in industrial situations.

Product Type	Wood preservative (PT 8)
Product name	ACTICIDE® OTW 8
Packaging	200 or 1000 L bulk containers
Categories of User	Industrial
Organisms controlled	Blue stain fungi and mould
Formulation type	Emulsion in water (EW) formulation
Concentration in formulation	8 %
Application method/kind	Dipping or vacuum pressure impregnation.
In use concentrations	250 ppm OIT in dipping/immersion treatment solution 150 ppm OIT in vacuum-pressure impregnation solution
Application number min/max	Single application
Storage	Use polyolefin containers

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

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

Appendix III: List of Studies

Please refer to separate reference documents.