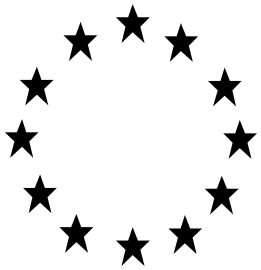
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Dinotefuran

Product-type 18
(Insecticides, acaricides and to control other arthropods)

17 June 2014

UK

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1 STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1 PROCEDURE FOLLOWED

This assessment report has been established as a result of the evaluation of the new active substance dinotefuran as product-type 18 (Insecticides, acaricides and products to control other arthropods), carried out in the context of Regulation (EU) No 528/2012, with a view to the possible approval of this substance.

On 29/03/2012 the UK competent authority received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 31/05/2012.

On 15/10/2013 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.

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 dinotefuran for product-type 18, and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

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

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

1.3 PRESENTATION OF THE ACTIVE SUBSTANCE

1.3.1 IDENTITY, PHYSICO-CHEMICAL PROPERTIES AND METHODS OF ANALYSIS

The main identification characteristics and the physico-chemical properties of dinotefuran are given in Appendix I to this document. The active substance must be technically equivalent to the specification given in the confidential annex for the active.

Dinotefuran is a white odourless crystalline solid, with a melting point of *ca* 108 °C; a boiling point could not be determined since the substance decomposed at 208 °C. With a vapour pressure of 5 x 10^{-5} Pa at 25 °C, it can be considered as not volatile. Dinotefuran is not surface active but is readily soluble in water; the solubility was not significantly affected by pH. The log octanol/water partition co-efficient was -0.64 at pH7 therefore the active substance does not have the potential to bio accumulate. Dinotefuran is not classified with regard to flammability and explosive properties; however it demonstrates oxidising properties on the basis of test method EC A17. A non-GLP test conducted according to the UN GHS test indicates that dinotefuran does not demonstrate oxidising properties.

The effects of temperature on the solubility in organic solvents and partition coefficient were not studied.

Details of the methods of analysis supporting the batch analysis are given in Appendix 1 to this document. An HPLC-UV method is available for the determination of the active in the technical material. This method has not been fully validated in terms of SANCO 3030/99 as for precision 3 determinations were made instead of the expected 5, however the method is considered acceptable.

The methods used to determine the impurities in the technical material have not been fully validated as for precision 3 determinations were made instead of the expected 5, however the method is considered acceptable.

An HPLC-UV/DAD method of analysis is available for the determination of dinotefuran in soil. The method is acceptably validated according to EU guidance in terms of linearity, accuracy, repeatability and reproducibility and is considered acceptable as a monitoring method; however a confirmatory technique is not available. A method of analysis for the determination of dinotefuran in water was provided using HPLC-MS/MS which could be used as a confirmatory technique if needed. The method is considered acceptable as a monitoring method. The LOQ of 0.01 mg/kg is considered sufficient.

An HPLC-MS/MS method of analysis is available for the determination of dinotefuran in water. The LOQ was 0.1 µg/L. The method was validated for drinking water, ground water and surface water. The method is considered acceptably validated for one ion transition only. Validation data for a second ion transition would be required in order to fully meet the requirements. The LOQ of 0.1 µg/L is considered sufficient as the $PNEC_{water}$ for dinotefuran is 0.254 µg/L.

A method is not required for air as the vapour pressure of dinotefuran was estimated to be < 1.7 x 10^{-6} Pa at 30 °C. Furthermore application by spraying is not envisaged therefore a method of analysis for air is not required.

A method is not required for the determination of residues in animal and human body fluids and tissues as dinotefuran is not classified as toxic or very toxic.

A method is not required for the determination of residues in food or feeding stuffs as proposed use pattern will not result in contact with food or feeding stuff.

Dinotefuran is intended for indoor use, as a spot treatment or to treat crevices in buildings and is not intended to be placed on in or near soils in agricultural or horticultural use.

1.3.2 INTENDED USES AND EFFICACY

Dinotefuran is an active substance proposed for use as an insecticide in Product Type 18 of the Biocidal Products Regulation.

Insecticidal products containing dinotefuran are for use in the control of cockroaches (i.e. *Blattella germanica*, *B. orientalis*).

Dinotefuran exerts its biocidal effect by acting as an agonist of insect nicotinic acetylcholine receptors, but it is postulated that dinotefuran affects the nicotinic acetylcholine binding in a mode that differs from other neonicotinoid insecticides.

The Applicant has provided the following statement describing the mode of action of dinotefuran.

> '*Dinotefuran is a neonicotinoid in the nitroguanidine class. It appears that dinotefuran acts as an agonist of insect nicotinic acetylcholine receptors, but it is postulated that dinotefuran affects the nicotinic acetylcholine; binding in a mode that differs from other neonicotinoid insecticides. Rapid knockdown and death occur within several hours after contact or ingestion of dinotefuran*'.

The Applicant has provided the following statement in support of their contention that the resistance of cockroaches to dinotefuran is not an issue.

> '*Dinotefuran is a nitroguanidine compound included with other insect nicotinic acetylcholine receptor (nAChRs) agonists in the Insect Resistance Action Committee (IRAC) group 4A. Detailed mode of action studies suggest that dinotefuran binds to the acetylcholine receptor site in a mode that differs to the chlorinated neonicotinic molecules included in IRAC group 4A. Attached is a summary of key findings from open literature that can be provided if required. In common with all insecticides the possibility of the development of a cross resistance or a specific resistance to dinotefuran cannot be discounted.*
>
> *Monitoring of resistance to dinotefuran from its extensive use in agricultural pest control has not indicated a significant cross or direct resistance problem that the manufacturers are aware of apart from one instance in Colorado potato beetle in the United States (http://www.pesticideresistance.com/search.php) but the recommended uses of dinotefuran follow IRAC practices to avoid resistance development which are fully supported by the manufacturer Mitsui Chemicals Agro, Inc.*
>
> *Strategies to reduce the risk of resistance developing such as recommendations to treat to levels that ensure complete kill of target pest infestations and to use dinotefuran*

alternately with substances with a different mode of action can be implemented at end-use product approval. Similarly, monitoring programs to confirm that target pests remain susceptible to dinotefuran will need to be implemented in relation to product approvals as target pests will vary with product and geography.

An IRAC poster concerning resistance and management of resistance in cockroaches, which is pertinent to the reference product in the dossier to support active substance approval, is provided.'

The biocidal formulation, Dinotefuran 2 % bait, is for professional use only and is supplied ready-to-use in a syringe style applicator tube. It is intended for indoor use only as a spot treatment to control cockroaches. It is not intended for outdoor use or for use where there is a risk of contamination to food or feed stuffs.

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.

1.3.3 CLASSIFICATION AND LABELLING

1.3.3.1 CURRENT ACTIVE SUBSTANCE CLASSIFICATION

There is no current harmonised classification for the active substance dinotefuran according to Annex VI of Regulation (EC) no 1272/2008.

1.3.3.2 PROPOSED ACTIVE SUBSTANCE CLASSIFICATION

Table 1.1 Proposed classification of dinotefuran based on Directive 67/548/EEC

Hazard symbol:	O N
Indication of danger:	Oxidising Dangerous for the environment
R-phrases:	R8 Contact with combustible material may cause fire R50/53 Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment

Table 1.2 Proposed classification of dinotefuran based on CLP Regulation

Pictogram:	
Signal word:	WARNING
Classification:	Aquatic acute 1

	Aquatic chronic 1
H-Statements:	H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects
M-Factors:	Aquatic acute: 10 Aquatic chronic: 10

1.4 SUMMARY OF THE RISK ASSESSMENT

1.4.1 HUMAN HEALTH RISK ASSESSMENT

1.4.1.1 HAZARD IDENTIFICATION

1.4.1.1.1 Toxicology Hazard Summary

Toxicokinetics

The results of the absorption and excretion studies demonstrate that ^{14}C-dinotefuran is well absorbed from the G.I. tract of male and female adult and neonate rats into the systemic circulation and is rapidly excreted mainly in the urine. Because extensive absorption has been demonstrated, an oral absorption value of 100 % will be used in the risk assessment. There are no significant differences in absorption and excretion in adult rats after single or repeated exposure and between high and low doses of dinotefuran. There is very limited enterohepatic re-circulation of dinotefuran as indicated by the low levels of radiolabel detected in the bile.

The tissue distribution studies on ^{14}C-dinotefuran demonstrate that following absorption from the G.I. tract the radiolabel is widely distributed in male and female adult and neonatal rats. In addition the distribution of dinotefuran and/or its metabolites extends to the foetus and to the milk of lactating rats. There is no evidence of bioaccumulation. The metabolite profiling studies demonstrate that only limited metabolism of dinotefuran occurs *in vivo* as <10 % of radiolabel is associated with metabolites. In addition similar metabolism pathways exist in adult males and females regardless of dosing regimen and in neonates.

Dermal absorption values

Dermal absorption values of 36 %, 27 % and 10 % were identified following 24 hours exposure to 0.03 %, 0.3 % and 3 % dinotefuran in an aqueous solution, in an *in vivo* study. However, the product is not an aqueous solution of dinotefuran so these values are considered inappropriate for this risk assessment. In the absence of product-specific data, a default dermal absorption value of 75 % (see http://www.efsa.europa.eu/en/efsajournal/pub/2665.htm) will be used.

Inhalation absorption values

No data are available to assess the absorption of dinotefuran following inhalation exposure. Therefore an inhalation absorption value of 100 % will be used for the risk characterisation process.

Acute toxicity, irritancy and sensitisation

For dinotefuran, oral LD_{50} values of 2804, 2000 and 2450 mg/kg are identified in rats for males, females and for the sexes combined, respectively. Similar values were identified in mice. In oral gavage rabbit developmental toxicity studies, clinical signs of toxicity were observed on the first day of dosing at 300 mg/kg and above; the NOAEL for acute effects in NZW rabbits is 125 mg/kg. The dermal LD_{50} value is estimated to be >2000 mg/kg and the

4 h inhalation LC_{50} value is estimated be > 4.09 mg/L in males and females. These data do not support classification of dinotefuran for acute toxicity. Dinotefuran is not a skin, eye or respiratory tract irritant or a sensitiser.

The product Dinotefuran 2 % Bait is not acutely toxic, does not cause skin, eye or respiratory tract irritation and is not a sensitiser.

Repeated dose toxicity

For the oral (dietary) route, the main toxic effects reported in all species tested (rats, mice and dogs) are reduced bodyweight gain and food consumption for subacute, subchronic and chronic exposures. The only evidence of target organ toxicity was the observation of increased cytoplasmic vacuolation of the adrenal cortex in a subchronic study in rats, although the adversity of this finding was considered as being questionable. The lowest oral dietary NOAEL is 22 mg/kg/day, observed in a subchronic (1 year) study in dogs.

For short-term oral gavage administration, investigated in developmental toxicity studies in rats and rabbits, reduced bodyweight gain and food consumption also occurred in both species. However, in rabbits these changes were accompanied by clinical signs (hypoactivity, prone position, panting, flushed nose and ears, and tremors in one study) and in one study by macroscopic pathology changes in the liver (pale discolouration) and stomach (gray-white plaque in fundus, thickened gastric mucosa), although the toxicological significance of the macroscopic changes is uncertain. The lowest short-term oral gavage NOAEL is 52 mg/kg/day, observed in rabbits.

By the dermal route, dinotefuran does not cause systemic or local toxicity on repeated subactute exposure.

By the inhalation route, dinotefuran causes reduced bodyweight gain and food consumption on repeated subacute (6 h/day) exposure in males only. A LOAEC of 0.22 mg/L is identified for males and NOAEC of 2.08 mg/L (the highest achievable concentration) is identified for females.

Classification for repeated dose toxicity is not appropriate because severe, irreversible, toxicity was not present at the guidance exposure levels given in the classification criteria of Directive 67/548/EEC and Regulation (EC) 1272/2008.

Mutagenicity

Dinotefuran tested negative in a bacterial reverse mutation assay, an *in vitro* mammalian cell gene mutation assay and in an *in vitro* chromosome aberration assay. Therefore it can be concluded that dinotefuran is not genotoxic.

Carcinogenicity

The carcinogenicity of dinotefuran has adequately been investigated in a standard rat chronic/carcinogenicity study and in a standard mouse carcinogenicity study. Both studies provided no evidence of carcinogenic activity. Therefore it is concluded that dinotefuran is not carcinogenic.

Reproductive toxicity

The developmental toxicity of dinotefuran has been investigated in standard oral (gavage) studies in rats and rabbits. Additionally, a developmental neurotoxicity study has been conducted. The potential adverse effects on fertility and general reproductive performance have been investigated in a standard oral (dietary) rat 2-generation study. These studies show that dinotefuran does not have the capacity to cause specific adverse effects on development, fertility or reproductive performance.

Neurotoxicity

The neurotoxicity of dinotefuran has been investigated in standard acute (oral gavage) and subchronic (oral dietary) neurotoxicity studies in adults and in a developmental neurotoxicity study. These studies showed that dinotefuran does not cause neurotoxicity in adults and is not a developmental neurotoxin.

Immunotoxicity

The immunotoxicity of dinotefuran has been investigated in a standard oral (dietary) study in the rat and mouse. No evidence of immunotoxicity, based on an assessment of the humoral T-lymphocyte-dependent response against antigen on SRBC, was observed. Additionally, no adverse effects on innate and humoral components of the immune system of F_1 pups were reported in a pilot developmental neurotoxicity study.

1.4.1.1.2 Reference values (systemic)

The risk characterisation is conducted by comparison of human exposure and the toxicity using the Acceptable Exposure Limit (AEL) approach in which the exposure estimates are compared with the systemic reference values that were determined by dividing the relevant N(L)OAEL (mg/kg/day) by an overall Assessment Factor (AF). Risks are considered acceptable if the systemic exposure/AEL ratio is < 1. Dinotefuran does not cause site of contact toxicity, reference values and a risk characterisation for local effects are not required.

The main systemic target for dinotefuran toxicity is bodyweight gain and food consumption on acute, subacute/subchronic (medium term) and chronic (long term) exposure. Dinotefuran is considered not to be genotoxic, carcinogenic, immunotoxic, neurotoxic or a reproductive toxin.

In relation to acute exposure, the most sensitive NOAEL is 175 mg/kg, based on the observation of clinical signs of toxicity on the first day of dosing in a NZW rabbit oral developmental toxicity study ([redacted] 1998e). This is considered to be an appropriate starting point for deriving a systemic AEL for acute exposure. In relation to medium term exposure, the most sensitive NOAEL is 22 mg/kg/day, observed in a 52 week oral subchronic study in dogs ([redacted] 1999c), which is considered to be the appropriate starting point for deriving a medium term systemic AEL. For long-term exposure, the most sensitive NOAEL is 100 mg/kg/day, observed in a 104 week oral study in rats ([redacted] 2000c). This exposure level is greater than the most sensitive NOAEL of 22 mg/kg/day for medium-term exposure in the dog. Because the adverse effects (reduced bodyweight gain and food consumption) elicited in the 52 week dog study did not become more severe as the study progressed, and a comparison of the results of the 13 week ([redacted] 1997c) and 104 week ([redacted] 2000c) studies in rat also show that the adverse effects of dinotefuran do not

become more severe with time, the NOAEL of 22 mg/kg/day is considered an appropriate starting point for both the medium and long-term AEL.

As the extent of oral absorption is considered to be 100 %, a correction factor is not needed in the derivation of systemic AEL values from data for the oral route.

There is no definitive information to identify the relative sensitivities to dinotefuran in humans and experimental animals. Similarly, there are no data to reliably inform on the potential for inter-individual variability in the susceptibility to the effects. Given these uncertainties, standard default assessment factors of 10 to account for potential inter-species variability and of 10 to account for intra-species variability will used in the AEL derivation. Additional assessment factors are not required because of the shape of the dose response curve (for example the dose response curves are not unusually shallow or very steep) or for severity of key adverse health effect.

Thus, the following systemic AELs are derived:

$\mathbf{AEL_{systemic,\ acute}}$ **= 1.75 mg/kg** (NOAEL of 175 mg/kg ÷ overall AF of 100)

$\mathbf{AEL_{systemic,\ medium\ term}}$ **= 0.22 mg/kg/day** (NOAEL of 22 mg/kg/day ÷ overall AF of 100)

$\mathbf{AEL_{systemic,\ long\ term}}$ **= 0.22 mg/kg/day** (NOAEL of 22 mg/kg/day ÷ overall AF of 100)

1.4.1.2 EXPOSURE ASSESSMENT

In line with the TNsG on Human Exposure to Biocidal Products (2002), the UK CA has carried out for this product, Dinotefuran 2 % bait and its specified uses, an exposure assessment for human health based on a tiered approach. The UK has started each exposure assessment using worst-case assumptions (e.g. assuming no personal protective equipment is worn). If the risks to human health following exposure to dinotefuran were considered to be acceptable following comparison of the predicted systemic dose with the appropriate NOAEL/NOAEC from animal studies, then no further refinement of the exposure scenario was carried out. If an unacceptable risk is identified for a particular exposure scenario, then a further refinement of the exposure/risk assessment was carried out using additional parameters (e.g. additional PPE etc.).

1.4.1.2.1 Primary exposure

Professional users

The potential route of exposure for the professional operator is via the dermal route through handling and during application. Primary exposure of professional operators during use of Dinotefuran 2 % bait will occur from application of the product using spot treatment or crack and crevice application (See Document IIB, section 3.2.3.1 for more details).

The Applicant has informed that a worker could apply the treatment once per hour during an average 8 hour day. As a professional operator could be using the product on a daily basis, this exposure scenario is regarded as long-term.

Exposures have been calculated for spot treatment and crack and crevice application of Dinotefuran 2 % bait. The exposure assessments are described in detail in Document IIB and the predicted primary exposures through professional use of Dinotefuran 2 % bait are summarised in Table 1.3 below.

Since the exposure to the SVC has been calculated and found to be acceptable. The exposure to professionals via inhalation will not be more than the SVC and so will also be acceptable.

Tier 1 assessment

The tier 1 assessment reflects the worst-case exposure scenario and so no PPE has been used.

Tier 2 assessment

In the tier 2 assessment, gloves have been accounted for with a penetration factor of 10 %.

Table 1.3 Summary of primary exposure assessments for professional uses of Dinotefuran 2 % bait

Exposure Scenario		**Estimated Internal Exposure**			
		estimated oral uptake (mg a.s./kg bw/day)	**estimated inhalation uptake (mg a.s./kg bw/day)**	**estimated dermal uptake (mg a.s./kg bw/ day)**	**estimated total uptake (mg a.s./kg bw/day)**
Spot treatment and crack and crevice application					
Tier 1 (no PPE)	Professional applying dinotefuran 2 % bait as a spot or crack and crevice treatment. (long-term).	NA	NA	0.2	0.2
Tier 2 (gloves)		NA	NA	0.02	0.02

Non-Professional users

No non-professional applications have been applied for.

1.4.1.2.2 Secondary exposure

Given that the product is used in cracks/crevices/voids and not on open or exposed surfaces then one could consider secondary exposure to the gel bait to be relatively unlikely. However, it is still necessary to assess exposure/risk to the gel and so reverse reference calculations have been carried out for completeness.

The potential routes of exposure for the general public are via the dermal, oral and inhalation routes. This is through contact with the applied gel, dislodged residue or from living or working in the building post application.

It is proposed that occupants of treated premises could potentially be dermally exposed to the gel should they be in contact with applied gel or gel that has become dislodged from treated areas. If infants came into contact with dislodged or applied gel, they could contaminate their hands and ingest the gel. The gel bait will contain 0.01% bittering (aversive) agent that could discourage ingestion. Both of these scenarios are considered to be acute exposure scenarios. In addition, occupants of treated premises could be exposed to vapours volatilised from the gel on treated surfaces. Adults, children and infants could inhale the vapours when in enclosed unventilated spaces. This would be a long-term exposure scenario and in a worst-case situation, occupiers could be exposed to air saturated with these vapours for 24 hours a day.

A summary of the estimated systemic exposures to dinotefuran arising from these scenarios is presented in Table 1.4.

Table 1.4 Summary of secondary exposure assessments

Exposure Scenario	**Estimated Internal Exposures**			
	estimated oral uptake (mg a.s./kg bw/day)	**estimated inhalation uptake (mg a.s./kg bw/day)**	**estimated dermal uptake (mg a.s./kg bw/day)**	**estimated total uptake (mg a.s./kg bw/day)**
Secondary inhalation exposure to occupants of premises (long-term)				
Adult	NA	0.001034	NA	0.001034
Child	NA	0.001661	NA	0.001661
Infant	NA	0.001836	NA	0.001836

Exposure Scenario	**Amount of gel required to reach AEL (mg product / day)**	**Number of gel spots required to reach AEL**
Secondary dermal exposure to dislodged or applied gel (Acute)		
Adult	7000	70
Child	4013.4	40.2
Infant	1166.6	11.6
Secondary oral exposure to dislodged or applied gel (Acute)		
Infant	875	8.8

1.4.1.2.3 Combined exposure

The UK CA considers that none of the primary and secondary exposure scenarios described realistically warrants a combined assessment.

1.4.1.3 RISK CHARACTERISATION

1.4.1.3.1 Primary exposure

Professional users

One professional exposure scenario has been identified, which is the application of Dinotefuran 2 % Bait using spot treatment and crack and crevice application. The risks are considered to be acceptable at the tier 1 exposure assessment, which assumes that no PPE is used; at this level the systemic exposure/AEL ratio is 0.91.

Since the exposure to the SVC has been calculated and found to be acceptable. The exposure to professionals via inhalation will not be more than the SVC and so will also be acceptable.

Non-Professional users

No non-professional applications have been applied for.

1.4.1.3.2 Secondary exposure

The risks are considered to be acceptable for occupants of treated premises, who could be exposed to vapours from Dinotefuran 2 % Bait after its application; the systemic exposure/AEL ratios are 0.005 - 0.008 for these scenarios.

Three other secondary exposure scenarios are considered using the reverse reference method to calculate the number of spots of Dinotefuran 2 % Bait that an individual could come in contact with that would result in the acute systemic AEL being achieved.

Firstly, it is proposed that occupants of treated premises could potentially be dermally exposed to the bait should they be in contact with applied gel or gel that has become dislodged from treated areas; for adults, children and infants, respectively, contact with 70, 40.2 and 11.6 spots of Dinotefuran 2 % Bait could result in the systemic AEL being achieved.

Secondly, if infants came into contact with dislodged or applied gel, they could contaminate their hands and ingest the gel; the ingestion of 8.8 spots of Dinotefuran 2 % Bait would result in the systemic AEL being achieved.

As a further risk mitigation measure with regard to the oral route of exposure, a bittering agent (denatonium benzoate) will be included in the Dinotefuran 2 % bait formulation. This will be included at 0.01 %. It should be noted that some children under 3-4 years old may not be able to taste denatonium benzoate due to their sense of taste not yet having developed sufficiently; also, some older people do not develop the ability to taste denatonium benzoate. The ability to taste - or not to taste - the bittering agent is a reflection of the diverse nature of the human population. Its inclusion will deter some but not necessarily all individuals (e.g. in particular some children) from ingesting the product [Review by W. Klein-Schwartz of Maryland Poison Centre, Baltimore (Vet Hum Toxicol, 1991 Dec 33(6): 545-7); Study by Berning CK, Griffith JF and Wild JE (Fundam Toxicol, 1982 Jan-Feb; 2(1): 44-8]. The UK CA is of the view that the inclusion of a bittering agent in the product formulation at a level of 0.01 % will not have any adverse toxicological effects.

Because the three secondary exposure scenarios considered using the reverse reference method indicate that contact with, or the consumption of, a relatively low number of spots of Dinotefuran 2 % bait by infants would result in the acute systemic AEL being achieved, it is recommended that the product is labelled with the following phrases:

PREVENT ACCESS TO BAITS by children and animals

KEEP IN A SAFE PLACE

Eight spots is the maximum amount of product that could be applied in a square metre. However since this product should be applied in cracks and crevices where insects hide, in the void areas and not on open surfaces; the product should not be in places that are easily accessible. If the product is applied as per the instructions on the label, it would seem unlikely that the exposure level would be achieved.

1.4.1.3.3 Combined exposure

The UK CA considers that none of the primary and secondary exposure scenarios described realistically warrants a combined assessment.

1.4.2 ENVIRONMENTAL RISK ASSESSMENT

1.4.2.1 FATE AND DISTRIBUTION IN THE ENVIRONMENT

Table 1.5 Abbreviations to identify common breakdown products of dinotefuran

Abbreviation	Full chemical name
UF	1-methyl-3-(tetrahydro-3-furylmethyl) urea
MG	1-methylguanidine
DN-2-OH	1-(2-hydroxytetrahydro-3-furylmethyl)-3-methylguanidine
DN-3-OH	1-(3-hydroxytetrahydro-3-furylmethyl)-3-methylguanidine
BCDN	3-(methylamino)-9-oxa-2-aza-4-azoniabicyclo[4.3.0]non-3-ene
DN	1-methyl-3-(tetrahydro-3-furylmethyl) guanidine
MNG	1-methyl-2-nitroguanidine
NG	Nitroguanidine

Fate in the aquatic compartment

Dinotefuran has been shown to be hydrolytically stable at environmentally relevant pH of 4, 7 and 9 plus elevated temperature (50 °C) with predicted DT_{50} values all in excess of 1 yr (when corrected to 12 °C). Further testing under extreme alkaline conditions of pH 11 and 13 with elevated temperature gave rise to DT_{50} values (corrected to 12 °C) of >30 d and >3 d respectively. Whilst formation of a major hydrolysis product, UF, was observed at extremely high pH, this would have limited significance under normal environmental conditions of pH and temperature. Although several major metabolites (UF, MG, BCDN, DN-3-OH and DN-2-OH) were identified under maximised test conditions (sterile solution buffered to pH 7 under constant irradiation) and seasonal DT_{50} values between 1.80 – 7.76 d were predicted at 40 °N from the available data after adjustment for natural sunlight, photolysis was not considered to be a major route for removal of dinotefuran. Turbidity of surface waters and indoor use patterns proposed for the representative product make it difficult to accurately predict the influence of photolysis in such systems on an EU-wide basis but in Northern European scenarios (similar to UK conditions at 50 – 58 °N), it is likely that photolysis will only have a relatively minor impact on removal from the aquatic compartment.

Based on the data provided, dinotefuran was not shown to be readily biodegradable, with 0 % degradation after 28 d based upon consumption of oxygen, but was reported to slowly break down (DT_{50} of 88.3 d (pond system) and 112 d (river system) at 12 °C; k = 0.0079 d^{-1} and 0.0062 d^{-1} respectively) to a single major metabolite, DN, which further degraded to CO_2 in aerobic sediment/water systems. DN was reported to reach a maximum level of

32.6 % AR in the pond system after 103 d and 23.1 % AR in the river system after 180 d. Non-extractable residues increased steadily throughout the study, reaching maximums of 62.9 % AR (pond system) and 28.2 % AR (river system) after 320 d. Significant levels of mineralisation were observed, reaching maximum levels of 19.9 % AR as $^{14}CO_2$ (pond system) and 34.9 % AR as $^{14}CO_2$ (river system). Half-lives for degradation of the metabolite DN were determined as 165 d (pond system) and 199 d (river system) when corrected to 12 °C.

No data were submitted to address bioconcentration potential of dinotefuran in the aquatic compartment on the basis that this would be unnecessary due to a reported log K_{ow} of -0.549 at pH 7 and 25 °C. In support of this, QSAR modelling performed in accordance with guidance in the "Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC (new notified substances), Commission Regulation (EC) No 1499/94 (existing substances) and Directive 98/8/EC (biocidal products)" (EC, 2003). A calculated BCF_{fish} value of only 0.06 strongly suggests a low potential to bioconcentrate and hence bioaccumulate in fish (QSAR modelling also suggests a similar lack of bioconcentration in earthworms with an estimated BCF <1). In addition, predicted log K_{ow} values for its major metabolites MNG (soil) and DN (aquatic compartment) were determined as -1.17 and -0.18 respectively and indicate that neither compound would be likely to bioaccumulate.

Fate in air

The fate of dinotefuran in air was investigated using the quantitative structure activity relationship estimation method (AOPWIN v.1.70; 1995 and corrected in line with defaults taken from TGD; 2003) which considers the reaction with the daily air concentrations of hydroxyl (OH^-) radicals. A maximum estimated half-life of 2.4 h was predicted but, as the active substance is not considered to be volatile as indicated by the reported vapour pressure of 5.0×10^{-5} Pa (at 25 ºC), the air compartment is not considered further in the exposure assessment.

Fate in the terrestrial compartment

Biodegradation of dinotefuran was investigated under aerobic conditions in a single European soil type (silt loam with 1.8 % of OC) at two different temperatures (10 °C and 20 °C) as an initial study to investigate potential degradation under more relevant environmental conditions than those used in biodegradability studies. Dinotefuran was shown to break down reasonably quickly with a DT_{50} of 19.2 d (corrected to 12 °C) to form a single major metabolite, MNG. MNG was also shown to degrade further (estimated DT_{50} of 137 d corrected to 12 °C) but at a much slower rate than its parent to form NG. Mineralisation was significant by study completion (120 d), with levels of $^{14}CO_2$ reaching 52.1 % AR (20 °C study) and 43.7 % AR (10 °C study). Therefore, the half-lives determined for dinotefuran and MNG are considered as appropriate worst-case values for use in an environmental risk assessment for refinement of exposure values where applicable.

A further anaerobic soil degradation study in a single European soil (silt loam with 1.78 % OC) at a single temperature (20 °C) was performed and dinotefuran did break down slowly (DT_{50} of 146 d corrected to 12 °C) to form DN as major metabolite. Another transformation product, UF, was detected but maximum levels only reached 7.7 % AR at study completion (120 d). Due to lack of reported degradation during the study, reliable half-lives for DN and UF could not be determined. It should be noted that anaerobic degradation of dinotefuran in

soil did not produce identical metabolites to those formed under aerobic conditions but mirrored the route of degradation demonstrated in the water-sediment study. Formation of DN and UF might not be directly as a result of unique soil reactions in the absence of oxygen as it is noted that soil samples were flooded prior to (anaerobic) incubation under nitrogen. However, it has been suggested that in water-sediment studies, the overlying water is aerated but in a manner to avoid disturbance to the sediment layer and so only the sediment surface may be considered as aerobic. If underlying sediment can therefore be considered anaerobic, then DN (and ultimately UF) would most likely form in anoxic conditions and not be significant aerobic degradates.

The adsorption and desorption of dinotefuran has been shown to be influenced by the organic content of the soil matrix. The arithmetic mean K_{OC} value of 31.4 $L.kg^{-1}$ (from the advanced study using 5 different soil types) suggests that the compound would not adsorb strongly to soil and would very easily undergo desorption, suggesting a potential for high mobility in the soil compartment. Due to the limited use pattern of the representative product (with indoor application to difficult to access areas for cockroach control), emissions to soil are extremely unlikely and therefore no consideration of potential soil metabolites has been considered necessary.

Overall, the available fate and behaviour studies suggest that dinotefuran would be subject to removal from the soil compartment as a result of aerobic degradation to MNG plus minor transformation products, ultimately leading to bound residues and subsequent mineralisation to CO_2. The parent compound would also be subject to mobility pressures, which would further remove any residues from this compartment. Therefore, the overall fate profile for this compound suggests that if exposure of the soil compartment were to occur, it is unlikely that accumulation in this compartment would take place.

The addition of a bittering agent at 0.01 % or a emulsifying agent at 0.5 % in the representative product does not trigger as a substance of concern for the environment according to the Directive. Therefore a formal quantitative risk assessment of these substances is not required and none has been performed. The risks arising from the product can be adequately determined based on the assessment of the active substance alone.

1.4.2.2 EFFECTS ASSESSMENT

Aquatic

The aquatic species shown to be most sensitive to dinotefuran was the chironomid (*Chironomus riparius*) following both acute and chronic exposure. The acute 48 h LC_{50} was 72.1 µg/l and the 27 d NOEC was 2.54 µg/l. These results are consistent with the opinion that daphnids (the most usual aquatic invertebrate tested) are not as susceptible to neonicotinoid insecticides as other invertebrates. Information on endpoints for other neonicotinoids (e.g. imidacloprid, clothianidin) is available in the EFSA conclusions/Review Reports which can be accessed via http://www.efsa.europa.eu/en/publications/efsajournal.htm#Conclusion and http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=activesubstance.selection. End points (L or EC_{50} as appropriate) for rainbow trout, daphnia, algae and Lemna were >100, >1000, >100 and > 110 mg/l respectively. Considering the sensitivity of *C. riparius* and that the chronic study was performed using spiked water (rather than spiked sediment), the $PNEC_{water}$ was calculated using the NOEC from the chronic test with this species and in

consultation with the TGD an assessment factor of 10 was applied. The resulting $PNEC_{water}$ of 0.254 µg/l has been used for risk assessment.

DN phosphate demonstrates similar toxicity to dinotefuran for the aquatic organisms for the base set acute data with all three tests (fish, algae & daphnia) performed as limit tests with end points of > 100 mg/l. Following the TGD, an assessment factor of 1000 was used to calculate the $PNEC_{water}$ of 0.1 mg/l.

Dinotefuran was demonstrated to have no inhibitory effect on aquatic microbial activity. An activated sewage sludge respiration inhibition test was performed and a NOEC of 1000 mg/l was determined. In accordance with the TGD, an assessment factor of 10 was applied to give a $PNEC_{STP}$ of 100 mg/l.

The toxicity of dinotefuran to sediment dwelling organisms was documented in a single long-term study with *Chironomus riparius* (NOEC 2.54 µg/l). The test was performed with spiked water and results suggested that most of the test item remained in the water rather than entering the sediment. Consequently, it was considered that the equilibrium method would be appropriate for calculating the $PNEC_{sed}$. However, the trigger value for no sediment effects assessment in the TGD is a Koc <500-1000 $L.kg^{-1}$. Dinotefuran has a Koc of 31.4 $L.kg^{-1}$. Therefore, the calculation of the $PNEC_{sed}$ is not required.

The toxicity of DN phosphate to sediment dwelling organisms was documented in a single study with *C. riparius* using spiked sediment (NOEC 5 mg/kg). In accordance with the TGD, the end point from this study was used to calculate the $PNEC_{sed}$ applying an assessment factor of 100. The resulting $PNEC_{sed}$ was 0.05 mg/kg.

Atmosphere

No data were submitted due to the intended use of the substance and the likelihood of exposure.

Terrestrial

Two studies were submitted to demonstrate the effects of dinotefuran on soil dwelling organisms. End points were available from a 56-day earthworm reproduction study (NOEC 0.2 mg/kg dry wt, 0. 0176 wet wt) and from a soil respiration and nitrification test using a 20 % SG formulation (NOEC 4 mg a.s./kg dry wt or 3.5 mg a.s./kg wet weight). As discussed at the working group meeting an assessment factor of 100 was deemed appropriate to determine the PNEC and the $PNEC_{soil}$ calculated to be 0.00176 mg/kg wet weight soil. The PNEC soil was also determined using the Equilibrium Partitioning Method and determined to be 0.00017. Since this value is smaller than that derived from the data it should be used in the risk assessment.

No data were submitted on terrestrial plants or birds due to the intended use of the substance and the likelihood of exposure.

The exposure assessment in the CAR is based on a very limited exposure. If in future applications (product authorisation) additional uses with soil exposures are claimed these need to be further assessed and additional data on soil living insects and NTAs are triggered.

Primary and secondary poisoning

In relation to primary poisoning, no assessment has been considered necessary. Although criteria stated within Chapter 5 of the "Emission Scenario Document for insecticides, acaricides, and products used to control other arthropods for household and professional use" [ENV/JM/MONO(2008)14] indicates that primary poisoning could occur when "*insecticides are applied together with food attractant*", the representative product would be applied indoors as a spot treatment in locations that would be difficult to access. In addition, it is not believed that gel products (such as Dinotefuran 2 % Bait) would be in a form that could be sufficiently appetent to birds or mammals so they would be at risk.

The potential for bioaccumulation was estimated from the log K_{ow}. With a value of -0.64, dinotefuran does not reach the accepted trigger value of ≥3 and this indicates a low potential for bioaccumulation. Major metabolites MNG (soil) and DN (aquatic compartment) have predicted log K_{ow} values of -1.17 and -0.18 respectively so are also not expected to bioaccumulate. Consequently, further consideration of the risk of secondary poisoning was unnecessary.

Bittering agent

The addition of a bittering agent at a level of 0.01 % in the representative product does not give rise to concerns with regard to ecotoxicology.

1.4.2.3 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".

<u>Persistence</u>

Results from a ready biodegradation study (where 0 % degradation was determined after 28 d) indicate that the P criterion cannot automatically be discounted (as outlined in screening criteria taken from Chapter R11 – PBT Assessment of the ECHA (REACH) Guidance on information requirements and chemical safety assessment).

Data have been presented that show that dinotefuran did degrade albeit relatively slowly in the aquatic environment with a worst-case DT_{50} value of 112 d for total river system (and 88.3 d in total pond system) at 12 °C under aerobic conditions in a sediment/water system. Furthermore, water phase dissipation DT_{50} values of 93.3 d (river system) and 43.6 d (pond system at 12 °C were also calculated. Therefore, dinotefuran does appear to fulfil the criteria for a persistent compound according to the TGD (>40 d in freshwater and/or >120 d in freshwater sediment). Furthermore, worst case dissipation DT_{50} values for river system also exceed criteria for very persistent compounds (>60 d in freshwater and/or >180 d in freshwater sediment) although values for freshwater (pond system) and freshwater sediment do not trigger additional concern. Based upon available data, a clear argument can be made to classify the active substance as "Persistent" (P) based upon total system degradation and "Very Persistent" (vP) based upon water phase dissipation. However, it is

noted that these conclusions have been based upon limited data (where n=2) such that highest DT_{50} values have been used in decision making.

The rate of degradation of the major metabolite, DN, was shown to be much slower in the aquatic environment, with a DT_{50} of 165 d (total pond system) and 199 d (total rivers system) reported at 12 °C. Therefore, this metabolite could also be of concern with regard to persistence in the aquatic environment and may need to be considered further if extensions to the use pattern of dinotefuran give rise to significant increases in emissions to surface waters. Currently, the representative product will only be applied indoors to difficult to access areas where wet cleaning is unlikely to occur and therefore discharges to STP and ultimately water bodies can be considered negligible.

Soil degradation data indicates that dinotefuran degrades quickly in aerated soil, with a DT_{50} of only 19.2 d at a normalised temperature of 12 °C. Based upon ECHA Guidance on PBT Assessment where a $T_{½}$ >120 d in soil would trigger the P criterion, the active substance cannot be considered persistent in this compartment. Its major soil metabolite, MNG, was reported to have a DT_{50} of 137 d at normalised temperature and this compound could be of concern with regard to persistence in the terrestrial environment based upon limited data.

Based upon the limited data set supplied for dinotefuran, it would appear that the compound should currently be classified as vP.

Bioaccumulation

A substance is considered to have the potential to fulfil the criterion of bioaccumulation when the log K_{ow} exceeds 4.5, but as a log K_{ow} of -0.549 has been derived for dinotefuran, there is no trigger for an assessment of the bioaccumulation potential of this active substance in aquatic organisms. Confirmatory QSAR modelling based upon work by Veith *et al* taken from the TGD on risk assessment (EC, 2003) and Mackay BCF regression modelling (Mackay, 1982) undertaken by the Applicant) give rise to predicted BCF values for fish of <0.1 and, therefore, the bioaccumulation criterion is not fulfilled.

Toxic

According to the available data, the most sensitive chronic endpoint is that derived for the *Chironomus* 27-day study (NOEC 2.54 µg/l). Thus the trigger of <0.01 mg/l given in the TGD is exceeded and dinotefuran can be considered to have fulfilled the criterion for toxic.

PBT Conclusion

Even though dinotefuran may appear to fulfil two (vP and T) out of the 3 criteria that need to be considered, it can be accepted that it is neither a PBT nor a vPvB substance. However, it must be considered as a ”candidate for substitution”.

1.4.2.4 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’.

Dinotefuran has been identified as triggering both the 'T' and 'P' criteria (such that it will be classified as vP and T), but is not considered to require the 'B' criterion. Theoretically, dinotefuran will not pose a possible risk for long-range transport on the basis of an estimated atmospheric half-life of only 2.4 h (assuming a 12 h day and an OH radical concentration of 5.0E+5 OH-/cm^3 when estimated using the AOPWIN v 1.92 QSAR modelling tool). This conclusion is further supported by the compound's very low vapour pressure (5E-5 Pa at 25 °C), low predicted Henry's Law constant plus limited environmental exposure from current use patterns.

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

1.4.2.5 EXPOSURE ASSESSMENT

The environmental exposure assessment for dinotefuran has been produced using all available information. This has been taken from submitted studies and the Organisation for Economic Co-operation and Development (OECD) Task Force document; 5th Draft Emission Scenario Document (ESD) for "Insecticides, acaricides and products to control arthropods (PT 18) for household and professional use" (OECD, July 2008). Information and guidance was also taken from part II of the Technical Guidance Document on risk assessment (TGD; EC, 2003). Furthermore, information and decisions taken from TM-IV-2009, TM-I-2010 and TM-II-2010 regarding modifications to building size and number, along with application rates to crack and crevice areas plus cleaning efficiency have been taken into account. All calculations within the exposure scenario apply to dinotefuran only, as other constituents of the Dinotefuran 2 % Bait product formulation are not considered to be compounds of concern. With regard to metabolites, DN is only considered as a major metabolite (of concern) in the aquatic compartment whilst MNG is only considered of concern in the terrestrial (soil) compartment. A full list of input parameters used in the determination of PEC values resulting from use of the representative products are presented in Table 1.6.

Table 1.6 PEC input assumptions for assessment of emissions from representative product (Dinotefuran 2 % Bait)

Input/Parameter (units)	Data/Endpoint
Local population in catchment of STP (-)	10,000
Daily wastewater flow per inhabitant (l d^{-1} eq^{-1})	200
Effluent discharge rate of STP (l d^{-1})	2×10^6
Size of targeted treatment area within each domestic dwelling (m²) *	2.0
Size of targeted treatment area within each larger building (m²) *	9.3
Number of potential houses treated per catchment (-)	4000 (indoor)
Number of potential large buildings treated per catchment (-) *	300 (indoor)
Simultaneity Factor (%) based upon weekly treatment indoors	2.75 (indoor)
$F_{simultaneity}$ for weekly indoor re-application (worst case use pattern)	0.0275
Maximum % exposed to cleaning – gel bait (crack and crevice & spot treatment) *	3
Cleaning efficacy (F_{CE}) : crack, crevice and spot treatment to difficult to access areas *	0.03
Fraction to water at STP (derived by SimpleTreat in EUSES 2.1.2)	>0.996
Fraction to sewage sludge at STP (derived by SimpleTreat in EUSES 2.1.2)	3.91×10^{-3}
Fraction to air at STP (derived by SimpleTreat in EUSES 2.1.2)	1.65×10^{-9}
Sludge rate : rate of sewage sludge production at STP (kg d^{-1})	710

* Default values based upon decisions reached at TM-IV-2009, TM-I-2010 and TM-II-2010

The environmental exposure assessment for Dinotefuran 2 % Bait (an RFU gel bait formulation containing 2 % dinotefuran by weight) is based on indoor use by professional operators only, at a maximum rate of 0.8 g of product per m^2 (equivalent to 16.0 mg a.s. m^{-2}). The potential environmental releases of dinotefuran resulting from the use of the representative product will be limited as the sole intended target pest would be cockroaches with application by small syringe devices into crack, crevices and other areas not prone to frequent wet cleaning within domestic dwellings and larger public, municipal and commercial buildings. Waste product and used packaging are expected to be sent to landfill in domestic waste and have not been considered further.

The environmental emissions associated with the local scale are considered to present the worst-case scenario in terms of predicted environment concentrations (PECs). In the scenarios presented, the underpinning assumption is that the associated product, Dinotefuran 2 % Bait, will be used indoors only by professional operators and will be applied responsibly in such a way as to maximise the effectiveness of the treatment and minimise unnecessary exposure of non-target groups (people, animals and environment) by crack, crevice and spot treatment in difficult to access areas where cockroaches congregate, feed and seek harbourage. The potential environmental emissions identified are:

Indoor use only

1. Emissions from treated hard surfaces (spot treatment in difficult to access areas or crack and crevice treatment) as a result of wet cleaning resulting in:
    - Direct exposure to the sewage treatment plant (STP) compartment via drains with,
        i. indirect exposure to surface waters (including sediment) via STP effluent,
        ii. indirect exposure to soil compartment (including groundwater) via STP sludge application to land and

iii. indirect exposure to biota via surface waters (bioconcentration in fish leading to secondary poisoning of fish-eating birds).

Potential environmental releases of dinotefuran resulting from indoor use of the gel bait product by professional operators against cockroach infestations should only be associated with hard surface treatment. The major route of environmental exposure is considered to be that resulting from the wet cleaning of hard surfaces around cracks and crevices or where spots of gel have been applied. Where regular cleaning is essential or customary, it is extremely unlikely that this type of formulation would provide effective control due to potential losses between re-application so use of the product will be limited to difficult to access locations / areas.

Further to the above assumptions, the indirect environmental exposure via domestic waste disposal to landfill and/or commercial waste disposal to hazardous waste sites (as a result of disposal of used packaging plus waste product and dry cleaning such as vacuuming of treated areas) has not been considered in this exposure assessment. This is because this route of exposure is less likely to be of concern when compared to the direct exposure via the STP compartment. In addition, the effect of its dilution with other wastes, biodegradation of the active substance (a.s.) and the significant containment measures at landfill sites according to European Union (EU) waste regulations (EU Directive 99/31/EC) further reduce any potential concerns.

The PEC values for the main compartments of concern (i.e. excluding the air compartment and sediment compartment) resulting from indoor use of Dinotefuran 2 % Bait are presented in the following Tables 3.9 - 3.13. It should be noted that no consideration of sediment compartment has been included as both the $PNEC_{sediment}$ and $PEC_{sediment}$ would need to be calculated using the Equilibrium Partitioning Method using relevant PEC and PNEC values for surface waters. As a consequence, the PEC/PNEC ratios for surface water and sediment will be identical.

Table 1.7 PEC STP

Scenario	PEC_{STP} (in mg l^{-1})
Domestic housing : normal treatment	2.64×10^{-5}
Larger buildings : normal treatment	9.14×10^{-6}
Total (housing + large buildings) : normal treatment	3.55×10^{-5}
Domestic housing : heavy treatment	5.30×10^{-5}
Larger buildings : heavy treatment	1.84×10^{-5}
Total (housing + large buildings) : heavy treatment	7.14×10^{-5}

[Note : in line with discussions on potentially higher applications being made in at least one MS due to national working practises for preventive cockroach control, PEC_{STP} values assuming treatment of 4 m^2 (house) and 18 m^2 would be 7.07×10^{-5} mg l^{-1} (total : normal rate) and 1.40×10^{-4} mg l^{-1} (total : heavy rate). However, such issues on scale of use would be resolved at PA level due to the need to provide clear application instructions.]

No consideration of metabolite formation has been considered at STP as zero degradation is assumed during transit in wastewater and predictions using SimpleTreat modelling (based upon the lack of ready biodegradation exhibited by parent compound) assume zero biodegradation within the STP itself.

Table 1.8 PEC SURFACE WATER

Scenario	$PEC_{surfacewater}$ (in mg l^{-1})
Domestic housing : normal treatment	2.64×10^{-6}
Larger buildings : normal treatment	9.14×10^{-7}
Total (housing + large buildings) : normal treatment	3.55×10^{-6}
Domestic housing : heavy treatment	5.30×10^{-6}
Larger buildings : heavy treatment	1.84×10^{-6}
Total (housing + large buildings) : heavy treatment	7.14×10^{-6}

[Note : in line with discussions on potentially higher applications being made in at least one MS due to national working practises for preventive cockroach control, $PEC_{surfacewater}$ values assuming treatment of 4 m^2 (house) and 18 m^2 would be 7.07×10^{-6} mg l^{-1} (total : normal rate) and 1.40×10^{-5} mg l^{-1} (total : heavy rate). However, such issues on scale of use would be resolved at PA level due to the need to provide clear application instructions.]

With regard to the formation of metabolites in aquatic systems, only one major metabolite – DN – was detected at significant concentrations (i.e. >10 %) in the water-sediment degradation study. Comparison of surface water effects for dinotefuran and DN presented in section 4.3 of Document II-A indicate that the major metabolite is significantly less toxic to aquatic organisms than its parent. Therefore, it is clear that environmental risks are likely to be driven by the presence of the a.s. in aquatic systems rather than its degradation products and so calculation of DN concentrations in surface waters has not been considered relevant. However, by way of confirmation, the highest $PEC_{surface\_water}$ value for dinotefuran (7.14×10^{-6} mg l^{-1}) has been used to derive a notional worst case $PEC_{surface\_water}$ value of 5.55×10^{-6} mg l^{-1} for DN.

Table 1.9 PEC SEDIMENT

Scenario	$PEC_{sediment}$ (in mg kg^{-1})
Domestic housing : normal treatment	Not calculated*
Larger buildings : normal treatment	Not calculated*
Total (housing + large buildings) : normal treatment	Not calculated*
Domestic housing : heavy treatment	Not calculated*
Larger buildings : heavy treatment	Not calculated*
Total (housing + large buildings) : heavy treatment	Not calculated*

* as discussed, risks to sediment compartment will be based upon risks to surface waters.

With regard to the formation of metabolites in aquatic systems, only one major metabolite – DN – was detected at significant concentrations (i.e. >10 %) in the water-sediment degradation study.

Although no $PNEC_{sediment}$ values have been derived for parent, a value of 3.43×10^{-2} mg kg^{-1} wwt has been calculated for DN and therefore it would be necessary to derive relevant $PEC_{sediment}$ values for the metabolite using EPM. Taking the highest $PEC_{surface\_water}$ value for dinotefuran of 7.14×10^{-6} mg l^{-1}, a notional worst case $PEC_{surface\_water}$ value of 5.55×10^{-6} mg l^{-1} can be assumed. QSAR modelling (US-EPA EPISuite v.4.11) allows determination of sufficient values to derive a $K_{susp\text{-}water}$ value of 2.025 m^3 m^{-3} so a worst case $PEC_{sediment}$ of 1.26×10^{-6} mg kg^{-1} wwt can be determined for DN.

Table 1.10 PEC Soil

Scenario	$PECloca l_{soil}$ Ecosystem [mg kg^{-1} wwt]
Housing – normal rate	2.61×10^{-7}
Larger buildings – normal rate	9.07×10^{-8}
Housing and buildings – normal rate	3.52×10^{-7}
Housing – heavy rate	5.25×10^{-7}
Larger buildings – heavy rate	1.82×10^{-7}
Housing and buildings – heavy rate	7.08×10^{-7}

[Note : in line with discussions on potentially higher applications being made in at least one MS due to national working practises for preventive cockroach control, $PECloca l_{soil}$ values (ecosystem) assuming treatment of 4 m^2 (house) and 18 m^2 would be 7.02×10^{-7} mg kg^{-1} wwt (total : normal rate) and 1.39×10^{-6} mg kg^{-1} wwt (total : heavy rate). However, such issues on scale of use would be resolved at PA level due to the need to provide clear application instructions.]

It should be noted that whilst PEC_{soil} values have also been derived for grassland and arable land, these will only be used for groundwater assessment.

With regard to the formation of metabolites in the terrestrial compartment, only one major metabolite – MNG – was detected at significant concentrations (i.e. >10 %) under aerobic conditions in a soil degradation study using silt loam as test substrate. Maximum formation of MNG did not exceed 20 % AR and, due to controlled indoor use of the representative product, indirect emissions of dinotefuran to the terrestrial compartment are negligible (0.391 % sorption to sewage sludge).

However, there is concern that the major soil metabolite MNG may be persistent in soil so an additional quantitative assessment of potential soil concentrations of this metabolite has also been included. Using C_{sludge} values for dinotefuran and correcting for differences in molecular weight (202.2 : 118.1), soil PEC values of MNG in ecosystem, arable land and grassland can be calculated. A worst case PEC_{soil} value of 7.45×10^{-7} mg kg^{-1} wwt (ecosystem) has been determined for MNG.

Table 1.11 PEC Groundwater

Scenario	$PECloca l_{soil}$ Arable land [mg kg^{-1} wwt]	$PECloca l_{porewater}$ [mg l^{-1}]
Dinotefuran		
Housing and buildings – heavy rate	7.08×10^{-7}	2.65×10^{-7}
Major metabolite - MNG		

Housing and buildings – heavy rate	5.27×10^{-7}	2.11×10^{-7}

Predicted concentrations of dinotefuran and its major metabolite MNG in local soil can be used to crudely indicate groundwater levels in line with the appropriate porewater equation (67) presented in the TGD for risk assessment. However, the approach is very simplistic and takes no account of soil characterisation (neglecting consideration of transformation plus dilution in deeper soil layers) but provides a useful screening technique. If unacceptable concentrations are determined in local porewater, then FOCUS PEARL modelling would be required.

Results demonstrate concentrations of both dinotefuran and MNG in porewater of non-specific "agricultural soil" significantly below the current quality standard set at 0.1 µg l^{-1} by the EU Drinking Water Directive (98/83/EC) and thus negates the need for additional FOCUS groundwater modelling.

1.4.2.6 RISK CHARACTERISATION

Risks to local STP

Table 1.12 presents the indoor risk characterisation (PEC:PNEC) values for dinotefuran at local STP as a result of professional use of the insecticidal product, Dinotefuran 2 % Bait, indoors as a cockroach treatment in both domestic and commercial situations.

Table 1.12 Risk characterisation (PEC:PNEC) values for dinotefuran at local STP as a result of using Dinotefuran 2 % Bait indoors for domestic and commercial scenarios

Scenario	PEC (mg l^{-1})	PNEC (mg l^{-1})	PEC:PNEC
Domestic housing : indoor normal treatment	2.64×10^{-5}	100.0	2.64×10^{-7}
Larger buildings : indoor normal treatment	9.14×10^{-6}		9.14×10^{-8}
Combined housing & buildings : indoor normal treatment	3.55×10^{-5}		3.55×10^{-7}
Domestic housing : indoor heavy treatment	5.30×10^{-5}		5.30×10^{-7}
Larger buildings : indoor heavy treatment	1.84×10^{-5}		1.84×10^{-7}
Combined housing & buildings : indoor heavy treatment	7.14×10^{-5}		7.14×10^{-7}

[Note : in line with discussions on potentially higher applications being made in at least one MS due to national working practises for preventive cockroach control, PEC_{STP} values assuming treatment of 4 m^2 (house) and 18 m^2 would be 7.07×10^{-5} mg l^{-1} (total : normal rate) and 1.40×10^{-4} mg l^{-1} (total : heavy rate). Overall, risks would still remain acceptable as PEC/PNEC values would still be $< 2.0 \times 10^{-6}$ and any such issues on scale of use would be resolved at PA level due to the need to provide clear application instructions.]

From data presented, application of dinotefuran as an insecticide within the representative product, Dinotefuran 2 % Bait, in accordance with the proposed indoor use pattern does not pose an unacceptable risk to local STP micro-organisms.

As metabolites are not predicted to form during transit of wastewater and whilst dinotefuran remains at the STP, no assessment of their risk to micro-organisms has been required.

Risks to the aquatic compartment (surface waters)

Table 1.13 presents the indoor risk characterisation (PEC:PNEC) values for dinotefuran in surface waters as a result of professional use of the insecticidal product, Dinotefuran 2 % Bait, indoors as a cockroach treatment in both domestic and commercial situations.

Table 1.13 Risk characterisation (PEC:PNEC) values for dinotefuran in surface waters as a result of using Dinotefuran 2 % Bait indoors for domestic and commercial scenarios

Scenario	PEC (mg l^{-1})	PNEC (mg l^{-1})	PEC:PNEC
Domestic housing : indoor normal treatment	2.64×10^{-6}	2.52×10^{-4}	1.03×10^{-2}
Larger buildings : indoor normal treatment	9.14×10^{-7}		3.60×10^{-3}
Combined housing & buildings : indoor normal treatment	3.55×10^{-6}		1.40×10^{-2}
Domestic housing : indoor heavy treatment	5.30×10^{-6}		2.09×10^{-2}
Larger buildings : indoor heavy treatment	1.84×10^{-6}		7.24×10^{-3}
Combined housing & buildings : indoor heavy treatment	7.14×10^{-6}		2.81×10^{-2}

[Note : in line with discussions on potentially higher applications being made in at least one MS due to national working practises for preventive cockroach control, $PEC_{surfacewater}$ values assuming treatment of 4 m^2 (house) and 18 m^2 would be 7.07×10^{-6} mg l^{-1} (total : normal rate) and 1.40×10^{-5} mg l^{-1} (total : heavy rate). Overall, risks would still remain acceptable as PEC/PNEC values would still be < 0.06 and any such issues on scale of use would be resolved at PA level due to the need to provide clear application instructions.]

From data presented, application of dinotefuran as an insecticide within the representative product, Dinotefuran 2 % Bait, in accordance with the proposed indoor use pattern does not pose an unacceptable risk to aquatic organisms in surface waters.

Although one major metabolite, DN, was identified in the water-sediment degradation study, its aquatic PNEC indicates that the compound can be considered to be less toxic than the parent and so risk to aquatic organisms from application of the representative product would be driven by the a.s. alone. By means of confirmation, highest emissions of dinotefuran to surface waters (heavy rate ; total buildings) would equate to a notional worst case $PEC_{surface\_water}$ of 5.55×10^{-6} mg l^{-1} for DN. When compared to its $PNEC_{aquatic}$ of 1.0×10^{-1} mg l^{-1}, a PEC/PNEC ratio of < 6.0×10^{-5} can be derived for this metabolite. Risks posed by DN to the aquatic compartment are therefore considered acceptable. However, *if* a study with C. riparius was available for the metabolite then it *may* lower the endpoint.

Risks to the sediment compartment

The mean K_{OC} value derived for dinotefuran in an advanced soil adsorption / desorption study was determined to be 31.4 $L.kg^{-1}$ and, according to the TGD on risk assessment (p. 111), "*substances with a K_{oc} < 500 – 1000 L/kg are not likely sorbed to sediment (SETAC, 1993)*". Furthermore, dinotefuran is reported to have a water solubility of >39 g l^{-1} and a log Kow of only -0.64 at pH 7 and 20 °C. On that basis, the compound is not expected to accumulate in sediment in aquatic systems but remain in the water phase so no $PNEC_{sediment}$ has been derived.

Calculation of a value for the PEC in sediment could be performed using the Equilibrium Partitioning Method (EPM) to modify PEC values determined in surface waters using the appropriate equation outlined in the TGD for risk assessment. However, in order to characterise risk in the sediment compartment, an identical EPM calculation would need to be undertaken to derive PNEC sediment (using the PNEC value derived for surface waters).

As both $PEC_{sediment}$ and $PNEC_{sediment}$ will be derived using the same calculation to modify $PEC_{surfacewater}$ and $PNEC_{surfacewater}$, then the risks posed to sediment compartment (in the form of PEC/PNEC) will be identical to those posed to surface waters.

From data presented in Table 1.13, application of dinotefuran as an insecticide within the representative product, Dinotefuran 2 % Bait, in accordance with the proposed indoor use pattern does not pose an unacceptable risk to aquatic organisms in surface waters. As a consequence, acceptable risks can also be assumed in the sediment compartment.

With regard to the formation of metabolites in aquatic systems, only one major metabolite – DN – was detected at significant concentrations (i.e. >10 %) in the water-sediment degradation study. Although no $PNEC_{sediment}$ value has been derived for dinotefuran, a value of 3.43×10^{-2} mg kg^{-1} wwt has been calculated for DN and therefore it would be necessary to derive relevant $PEC_{sediment}$ values for the metabolite using EPM.

Taking the highest $PEC_{surface\_water}$ value for dinotefuran of 7.14×10^{-6} mg l^{-1} (heavy rate ; total emissions from housing and buildings), a notional worst case $PEC_{surface\_water}$ value of 5.55×10^{-6} mg l^{-1} has been determined. Overall, a worst case $PEC_{sediment}$ of 1.26×10^{-6} mg kg^{-1} wwt can be determined for DN and this gives rise to a worst case PEC/PNEC ratio of 3.67×10^{-5}.

Risks posed by DN to sediment dwelling organisms in the aquatic compartment are therefore considered acceptable.

Risks to the soil compartment

Table 1.14 presents the indoor risk characterisation (PEC:PNEC) values for dinotefuran in various soil compartments as a result of professional use of the insecticidal product, Dinotefuran 2 % Bait, indoors as a cockroach treatment in both domestic and commercial situations.

Table 1.14 Risk characterisation (PEC:PNEC) values for dinotefuran in local soil (terrestrial ecosystem) as a result of using Dinotefuran 2 % Bait indoors for domestic and commercial scenarios

Scenario	**PEC (mg kg^{-1})**	**PNEC * (mg kg^{-1})**	**PEC:PNEC**
Domestic housing : indoor normal treatment	2.61×10^{-7}	1.71×10^{-4}	1.53×10^{-3}
Larger buildings : indoor normal treatment	9.07×10^{-8}		5.30×10^{-4}
Combined housing & buildings : indoor normal treatment	3.52×10^{-7}		2.06×10^{-3}
Domestic housing : indoor heavy treatment	5.25×10^{-7}		3.07×10^{-3}
Larger buildings : indoor heavy treatment	1.82×10^{-7}		1.06×10^{-3}
Combined housing & buildings : indoor heavy treatment	7.08×10^{-7}		4.14×10^{-3}

*Although the soil PNEC for dinotefuran was originally determined as a dry weight (dwt) value, it has been revised to its equivalent wet weight value (in line with PEC values) by use of conversion factor of 0.8824: this is the factorial difference between RHO_{dry_soil} of 1500 kg m^{-3} and RHO_{wet_soil} of 1700 kg m^{-3}. However, a more precautionary approach has now been taken using a value derived by EPM.
[Note : in line with discussions on potentially higher applications being made in at least one MS due to national working practises for preventive cockroach control, $PEClocal_{soil}$ values (ecosystem) assuming treatment of 4 m^2 (house) and 18 m^2 would be 7.02×10^{-7} mg kg^{-1} wwt (total : normal rate) and 1.39×10^{-6} mg kg^{-1} wwt (total : heavy rate). Overall, risks would still remain acceptable as PEC/PNEC values would still be < 0.0005 and any such issues on scale of use would be resolved at PA level due to the need to provide clear application instructions.]

From data presented, application of dinotefuran as an insecticide within the representative product, Dinotefuran 2 % Bait, in accordance with the proposed indoor use pattern does not pose an unacceptable risk to terrestrial organisms in local soils.

Data concerning effects of the major soil metabolite, MNG, on soil dwelling organisms have not been provided as the Applicant has argued successfully for non-submission of data based upon a lack of direct exposure to this compartment from use of the representative product. Acceptance of the justification has been further supported by high margins of safety demonstrated for the parent compound when reaching soil via application of sewage sludge. However, as a crude screening method, PEC values determined for dinotefuran could be assumed for the metabolite MNG (which would be extreme worst case values as soil degradation studies indicated maximum formation of 16 % MNG based on AR). Furthermore, in the absence of effects data on terrestrial or aquatic organisms, it is commonly accepted under other EU legislation (such as EC Regulation No. 1107/2009 concerning plant protection products) to assume that metabolites could potentially be 10 times more toxic than their parent compound such that a PNEC value of 4.00×10^{-4} mg kg^{-1} dwt (or 3.53×10^{-4} mg kg^{-1} wwt) could crudely be set for MNG. Whilst this extremely conservative approach is not standard for assessment of biocidal active substances, it would offer an additional safeguard in a simplistic risk assessment, especially as MNG contains the nitroguanidine structure of the parent compound and therefore could be considered as possessing similar soil toxicity. Please note that it is being applied only on a case-by-case basis in relation to dinotefuran and does not reflect a change in procedure / policy for all biocidal active substances.

However, there is concern that the major soil metabolite MNG may be persistent in soil so an additional quantitative assessment of potential soil concentrations of this metabolite has also been included. Using C_{sludge} values for dinotefuran and correcting for differences in molecular weight (202.2 : 118.1), soil PEC values of MNG in ecosystem, arable land and grassland can be calculated. A worst case PEC_{soil} value of 7.45×10^{-7} mg kg^{-1} wwt (ecosystem) have been determined for MNG.

Overall, the highest possible PEC:PNEC value for MNG would be 2.11×10^{-4} (compared to parental $PNEC_{soil}$) or 2.11×10^{-3} (based on 10x soil toxicity of parent) – these clearly indicate acceptable risks for the terrestrial compartment.

The exposure assessment in the CAR is based on a very limited exposure. If in future applications (product authorisation) additional uses with soil exposures are claimed these need to be further assessed and additional data on soil living insects and NTAs are triggered.

Risks to groundwater

In soil, dinotefuran has the potential to be mobile (mean K_{OC} of 31.4 $L.kg^{-1}$) and can be shown to metabolise under aerobic conditions to the metabolite, MNG, which in turn forms bound residues in the soil compartment and significant mineralisation to CO_2. Therefore, it is reasonable to assume indirect exposure of groundwater (and even surface waters via run-off from fields). Guidance within relevant ESDs for insecticide use advocate calculating surface water concentration on the basis of porewater predictive modelling according to the method of Montfoort (1999) and assuming for first tier assessment that entry of run-off water into receiving water will undergo a ten-fold dilution.

Predicted concentrations of dinotefuran in local soil can be used to crudely indicate groundwater levels in line with equations presented in the TGD for risk assessment (EC, 2003) although this approach is very simplistic and takes no account of soil characterisation (by neglecting consideration of transformation plus dilution in deeper soil layers). A worst case PEC $local_{soil}$ (arable land) of 7.08×10^{-7} mg kg^{-1} wwt (derived from heavy infestation rate combining emissions from domestic houses and larger buildings) would predict a worst case $PEClocal_{soil,\ porewater}$ of 2.65×10^{-7} mg l^{-1} (i.e. 0.000265 µg l^{-1}). Whilst noted as being a simplistic approach, this value does represent a concentration in porewater of non-specific "agricultural soil" significantly below the current quality standard set at 0.1 µg l^{-1} by the EU Drinking Water Directive (98/83/EC) and negates the need for additional FOCUS groundwater modelling.

Initially, it was not considered necessary to perform an assessment to predict soil concentrations for the major soil metabolite, MNG, based upon application of sewage sludge to agricultural land as it is unclear whether significant levels will form as the parent compound (dinotefuran) may be highly mobile. If it were assumed as an "extreme worst case" assessment that degradation resulted in equivalent levels of MNG to those predicted in soil for dinotefuran, then risks to porewater from formation of the metabolite would fall significantly below the current quality standard (i.e. 0.1 µg l^{-1}) from the EU Drinking Water Directive (98/83/EC) and again negates the need for additional FOCUS groundwater modelling.

However, there is concern that MNG may be persistent in soil, based and so additional quantitative assessment of potential groundwater risk from this major soil metabolite has now been included. Although there will be some accumulation of MNG in soil due to slow

degradation, modelling predicts that this reaches a steady state after approximately 4 yr. Using C_{sludge} values for dinotefuran and correcting for differences in molecular weight, worst case soil PEC values of MNG in ecosystem, arable land and grassland can be calculated. PEC_{soil} values of 5.27 x 10^{-7} mg kg^{-1} wwt (arable) and 2.11 x 10^{-7} mg kg^{-1} wwt (grassland) have been determined for MNG when using the highest C_{sludge} rate (total emissions from housing and buildings following application of heavy rate).

Following the same approach taken for dinotefuran, screening in porewater by means of TGD equation (67) will be performed as a precursor to FOCUS PEARL modelling. Although limited endpoints are available for MNG, QSAR modelling has allowed determination of sufficient values (outlined in Table 1.14) to derive a $K_{soil\text{-}water}$ value of 4.25 m^3 m^{-3}.

Overall, a worst case $PEClocal_{soil,\ porewater}$ of 2.11 x 10^{-7} mg l^{-1} (i.e. 0.000211 µg l^{-1}) can be determined for MNG from levels predicted in arable land. Whilst noted as being a simplistic approach, this value does represent a concentration in porewater of non-specific "agricultural soil" significantly below the current quality standard set at 0.1 µg l^{-1} by the EU Drinking Water Directive (98/83/EC) and negates the need for additional FOCUS groundwater modelling.

However, it must be noted that groundwater levels of both dinotefuran and MNG can only be considered acceptable based upon limited indoor application of Dinotefuran 2 % Bait against cockroaches. Any change in use pattern, application rate etc would negate this assessment and will require additional porewater (or even FOCUS PEARL) modelling at product authorisation level.

Risks to non-target biota

No quantitative risk assessment has been carried out on non-target biota as environmental emissions are extremely low. It is noted that dinotefuran is a new furanicotinyl insecticide (reported to represent the third generation of neonicotinoid compounds) and could therefore potentially demonstrate toxicity to bees. However, due to controlled indoor application of the representative product, Dinotefuran 2 % Bait, by professional operators into difficult to access areas for cockroach control, direct releases to local soil are not expected. Furthermore, any emissions to agricultural land are only predicted to occur after wastewater discharges following limited wet cleaning of internal surfaces have reached the local STP and <0.1 % of a.s. has then sorbed onto sewage sludge. In addition, it is anticipated that sludge application to agricultural land will occur at a time when flowering plants are not evident (or in circumstances when flowering weeds will have been ploughed into the soil and thus unavailable to bees). On that basis, contact of bees with a.s. in the contaminated sewage sludge will be negligible and so no further assessment has been considered necessary.

In addition, risks for other non-targets such as birds and small mammals have not been considered because of the formulation and application type plus limited likelihood of emissions to the environment. The UK CA does not consider there to be a risk to biota because dinotefuran has a log K_{ow} of -0.64 and estimated BCF values of 0.06 (fish) and 0.83 (earthworms). Therefore, as the product will be used indoors in a controlled manner such that emissions to environment will be extremely low, dinotefuran is not expected to bioaccumulate in the environment. With regard to metabolites of dinotefuran, the major soil metabolite MNG is calculated as having a BCF (earthworm) of 0.83 whilst the major aquatic metabolite DN has a predicted BCF (fish) of 0.14. Neither metabolite is expected to

bioaccumulate in the relevant environmental compartment and so assessment of primary and secondary poisoning have not been considered necessary.

Therefore, changes to the formulation type, application / delivery method and use pattern will likely trigger the need for additional data and risk assessment to assess potential increases in risk to non-target biota at Member State level.

1.4.3 HUMAN HEALTH AND ENVIRONMENTAL RISK ASSESSMENT SUMMARY

1.4.3.1 PROFESSIONAL USERS

Table 1.15 Human Health, Companion Animal and Environmental Risk Assessment Summary

Human health risk assessment	
Exposure scenario	**Risk assessment**
Primary exposure (professional spot treatment and crack and crevice application)	Acceptable
Secondary exposure (occupants of treated premises exposed to vapours)	Acceptable
Secondary exposure (adult occupants of treated premises dermally exposed to 70 spots of dislodged or applied gel)	Systemic AEL achieved (reverse reference method)*
Secondary exposure (child occupants of treated premises dermally exposed to 40.2 spots of dislodged or applied gel)	Systemic AEL achieved (reverse reference method)*
Secondary exposure (infant occupants of treated premises dermally exposed to 11.6 spots of dislodged or applied gel)	Systemic AEL achieved (reverse reference method)*
Secondary exposure (infant occupants of treated premises ingest 8.8 spots of dislodged or applied gel via contaminated hands)	Systemic AEL achieved (reverse reference method)*
Environmental risk assessment (emissions from treated hard surfaces [spot treatment in difficult to access areas or crack and crevice treatment] as a result of as a result of wet cleaning)	
Exposure scenario	**Risk assessment**
Direct exposure to the sewage treatment plant (STP) compartment via drains	Acceptable
Indirect exposure to surface waters (including sediment) via STP effluent	Acceptable
Indirect exposure to soil compartment (including groundwater) via STP sludge application to land	Acceptable
Indirect exposure to biota via surface waters (bioconcentration in fish leading to secondary poisoning of fish-eating birds)	Acceptable

***** Because secondary exposure scenarios considered using the reverse reference method indicate that contact with, or the consumption of, a relatively low number of spots of Dinotefuran 2 % bait by infants and companion animals would result in the acute systemic AEL being achieved, it is recommended that the product is labelled with the following phrases: PREVENT ACCESS TO BAITS by children and animals, KEEP IN A SAFE PLACE

1.4.4 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.

Available evidence at this time indicates that dinotefuran does not meet these exclusion criteria as it is not classified or does not meet the criteria for classification as CMR 1A or 1B, does not have endocrine-disrupting properties and does not meet the criteria for PBT or vPvB. The conclusion that dinotefuran does not have endocrine-disrupting properties is based on the absence of significant effects on endocrine organs and/or reproduction in standard mammalian toxicity studies; it is noted that minimal or slight increased cytoplasmic vacuolation of the adrenal cortex was observed in a 13 week dietary study in the rat ([redacted] 1997c), but this was considered not to be a significant effect because, firstly, there were no correlating clinical pathology findings indicating the presence of a functional deficit and, secondly, changes in the adrenal cortex were not seen in any other dinotefuran toxicity study, including the chronic studies.

Article 10 (candidates 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 that 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.

With regard to toxicology, available evidence indicates that dinotefuran does not meet any of the a-f criteria of Article 10 and so should not be considered a candidate for substitution at this time.

With regard to the environment, available evidence at this time indicates that dinotefuran meets the conditions of criterion (d) of Article 10 since it is proposed to be classified as 'vP' and 'T'. In view of this dinotefuran may be considered in the future to be a likely candidate for substitution according to 528/2012.

1.4.5 ASSESSMENT OF ENDOCRINE DISRUPTOR PROPERTIES

The endocrine disrupting effects cannot be determined at present as the criteria are not yet agreed. However, in the absence of significant effects on endocrine organs and/or reproduction in standard mammalian toxicity studies it has been concluded that dinotefuran does not have endocrine-disrupting properties in mammals. In view of this it is reasonable to also expect that in mammalian wildlife and companion animals at least, endocrine disruption is not a concern.

1.5 LIST OF ENDPOINTS

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

1.6 OVERALL CONCLUSIONS

The outcome of the assessment for dinotefuran in product-type 18 is specified in the BPC opinion following discussions at the June 2014 meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA web-site.

Appendix I: List of endpoints

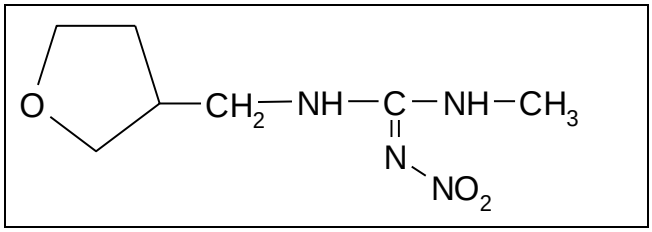
Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

Active substance (ISO Common Name)	Dinotefuran
Product-type	Product type 18
Applicant	LKC UK Ltd. Crowe Clark Whitehill LLP Carrick House Lypiatt Road Cheltenham GL50 2QJ United Kingdom Telephone: (41) 61 906 8501 Email: Dinotefuran.PT18@lkc-ltd.com

Identity

Chemical name (IUPAC)	(*RS*)-1-methyl-2-nitro-3-(tetrahydro-3-furylmethyl)guanidine
Chemical name (CA)	*N*-methyl-*N′*-nitro-*N″*-[(tetrahydro-3-furanyl)methyl]guanidine
CAS No	165252-70-0
EC No	Not available
Other substance No.	CIPAC number: 749
Minimum purity of the active substance as manufactured (g/kg or g/l)	991 g/kg dinotefuran
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None
Molecular formula	$C_7H_{14}N_4O_3$
Molecular mass	202.2 g/mole

Structural formula



Physical and chemical properties

Melting point (state purity)	107.5 °C (99.9 %)
Boiling point (state purity)	Not applicable (decomposition occurred before boiling)
Temperature of decomposition	208 °C (99.9 %)
Appearance (state purity)	White crystalline solid (99.6 %)
Relative density (state purity)	Density: 1.40 g/cm^3 (99.9 %)
Surface tension	72 mN/m at 20.2 °C ± 0.2 °C (99.2 %, 0.1 % solution)
Vapour pressure (in Pa, state temperature)	< 1.7 x 10^{-6} Pa at 30 °C (99.9 %) 5.0 x 10^{-5} Pa at 25 °C (99.5 %)
Henry's law constant (Pa m^3 mol $^{-1}$)	Not calculated. Vapour pressure could not be determined at 20 °C. Extrapolation by linear regression was not possible due to the lack of experimentally determined data points at other temperatures.
Solubility in water (g/l or mg/l, state temperature)	pH__5____: 52.3 g/L at 20 °C
	pH__7____: 54.5 g/L at 20 °C
	pH__9____: 51.2 g/L at 20 °C
	pH (purified water used) : 39.0 g/L at 10 °C 54.3 g/L at 20 °C 89.7 g/L at 30 °C
Solubility in organic solvents (in g/l or mg/l, state temperature)	solubility at 20 °C : Hexane: 9.0 µg/L Heptane: 10.5 µg/L Xylene: 71.85 mg/L Toluene: 148.6 mg/L Dichloromethane: 60.86 g/L Acetone: 57.84 g/L Methanol: 57.18 g/L Ethanol: 19.37 g/L Ethyl acetate: 5.17 g/L
Stability in organic solvents used in biocidal products including relevant breakdown products	Not applicable as the active is not manufactured/delivered in an organic solvent

Partition coefficient (log P_{OW}) (state temperature)	pH___5___: log P o/w = -0.915 at 25 °C
	pH___7___: log P o/w = - 0.644 at 25 °C
	pH___9___: log P o/w =-0.760 at 25 °C
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH_4__: >7 d (50 ºC) (equivalent to >1 yr at 12 °C) No degradation products detected
	pH_7__: >7 d (50 ºC) (equivalent to >1 yr at 12 °C) No degradation products detected
	pH_9__: >7 d (50 ºC) (equivalent to >1 yr at 12 °C) No degradation products detected Additional testing performed under extreme alkaline conditions (pH 11 plus pH 13) and elevated temperature demonstrated hydrolysis with formation of 1-methyl-3(tetrahydro-3-furlmethyl) urea at both pH. DT_{50} values were 45.0 h (pH 11 and 50 °C) plus 4.2 h (pH 13 and 50 °C).
Dissociation constant	No dissociation over pH range 1.4 – 12.3
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Tested at pH 2, 7 and 11. λ_{max} = 268 nm. Extinction coefficient (ε) at λ_{max} : pH 2 = 12,450 $M^{-1}cm^{-1}$ pH 7= 12,400 $M^{-1}cm^{-1}$ pH 11 = 11,200 $M^{-1}cm^{-1}$ No absorption maxima at or > 290 nm
Photostability (DT_{50}) (aqueous, sunlight, state pH)	DT_{50} = 1.80 – 7.76 d extrapolated for "seasonal" natural sunlight at 40 °N (or 1.97 – 18.60 d at 50 °N), major metabolites being UF, MG, BCDN and combined DN-2-OH & DN-3-OH (all >10 %), with up to 12 "minor" unidentified products that could not be isolated or identified separately.
Quantum yield of direct phototransformation in water at Σ > 290 nm	1.57×10^{-4}
Flammability	Not highly flammable

	Not auto-flammable
Explosive properties	Not explosive

Classification and proposed labelling

with regard to physical/chemical data	R67/548: O, R8 CLP: not classified
with regard to toxicological data	None
with regard to fate and behaviour data	N Dangerous for the environment R50/53 Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment Warning: Aquatic acute 1 Aquatic chronic 1 H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects
with regard to ecotoxicological data	None

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	HPLC-UV (270 nm)
Impurities in technical active substance (principle of method)	HPLC-UV (254 nm)

Analytical methods for residues

Soil (principle of method and LOQ)	Dinotefuran HPLC-UV/DAD 0.01 mg/kg HPLC-UV/DAD is not considered highly specific. The measurement technique used for water (LC-MS/MS) could be used as a confirmatory technique.
Air (principle of method and LOQ)	Not required as active is not volatile and the

	intended use does not include application via spraying
Water (principle of method and LOQ)	Dinotefuran HPLC-MS/MS 0.1µg/L Validation data provided for one transition only. Further data for a second transition may be required before product authorisation.
Body fluids and tissues (principle of method and LOQ)	Not required [substance is not classified as toxic (T) or very toxic (T^+)]
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not required as proposed use will not lead to contact with food/feeding stuff
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required as proposed use will not lead to contact with food/feeding stuff

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Rapid and extensive;100 % absorption assumed
Rate and extent of dermal absorption:	75 % absorption assumed, in the absence of product specific data
Distribution:	Widespread distribution to all tissues
Potential for accumulation:	Low
Rate and extent of excretion:	Rapid and extensive
Toxicologically significant metabolite(s)	None

Acute toxicity

Rat LD_{50} oral	2450 mg/kg bw (males and female rats, combined)
Rat LD_{50} dermal	>2000 mg/kg bw
Rat LC_{50} inhalation	>4.09 mg/L (4 hour exposure, nose only)
Skin irritation	Not irritating
Eye irritation	Not irritating
Skin sensitization (test method used and result)	Not a skin sensitiser (GPMT)

Repeated dose toxicity

Species/ target / critical effect	Rat, mouse, dog: no target organ identified, critical effect is reduced bodyweight gain & food consumption
Lowest relevant oral NOAEL / LOAEL	NOAEL 22 mg/kg bw/day (dietary 1 year dog study)

Lowest relevant dermal NOAEL / LOAEL	NOAEL 1000 mg/kg bw/day (the highest dose level tested, 28 day rat study)
Lowest relevant inhalation NOAEL / LOAEL	LOAEC 0.22 mg/L (6 hour/day exposure, 28 day rat study)

Genotoxicity

	Not genotoxic

Carcinogenicity

Species/type of tumour	Not carcinogenic (rat and mouse)
lowest dose with tumours	Not carcinogenic (rat and mouse)

Reproductive toxicity

Species/ Reproduction target / critical effect	No specific adverse effects on reproduction
Lowest relevant reproductive NOAEL / LOAEL	NOAEL 822 mg/kg bw/day (the highest dose level tested in 2-generation study)
Species/Developmental target / critical effect	No specific adverse effects on development
Lowest relevant developmental NOAEL / LOAEL	NOAEL 175 mg/kg bw/day (rabbit; the effects seen at this dose level were considered to be secondary to reduced maternal food consumption)

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	Not neurotoxic
Lowest relevant neurotoxicity NOAEL / LOAEL.	NOAEL 3413 mg/kg bw/day (the highest dose level testing in 13 week rat dietary study)

Other toxicological studies

	Negative in standard immunotoxicity study

Medical data

	No specific human symptoms of dinotefuran toxicity are known. Effects of human exposure to dinotefuran should be transitory and resolved 24 hours after exposure. The time between over-exposure and commencement of treatment should be as short as possible but is not expected to be crucial for the final health status.

Summary

	Value	Study	Safety factor
ADI	0.22 mg/kg bw/day	Dog oral (dietary) 1	100

		year study	
ARfD	1.75 mg/kg bw/day	Rabbit (NZW) oral developmental toxicity study	100
$AEL_{(systemic, acute)}$	1.75 mg/kg bw/day	Rabbit (NZW) oral developmental toxicity study	100
$AEL_{(systemic, medium term)}$	0.22 mg/kg bw/day	Dog oral (dietary) 1 year study	100
$AEL_{(systemic, long term)}$	0.22 mg/kg bw/day	Dog oral (dietary) 1 year study	100
Reference value for dermal absorption	75 %	Default value, as no product specific data	-

Acceptable exposure scenarios (including method of calculation)

Professional users

Exposure route: Dermal (long-term scenario)

Product(s): Dinotefuran 2 % bait (2 %)

Intended uses: Dinotefuran 2 % bait is a ready to use gel applied indoors by professionals against cockroaches (professional application: spot treatment and crack and crevice application of gel).

$AEL_{(systemic, long term)}$: 0.22 mg/kg/day

Method of calculation: AEL approach

Task	Tier	Exposure/AEL Ratio
Professional applying dinotefuran 2 % bait as a spot or crack and crevice treatment.	Tier 1	0.91
	Tier 2	0.09

Non-Professional users

No non-professional applications have been applied for.

Secondary (indirect) exposure as a result of use

Exposure route: Dermal (short-term scenario), oral (short-term scenarios) and inhalation (long-term scenario).

Product(s): Dinotefuran 2 % bait (2 %)

Systemic short-term AEL: 1.75 mg/kg bw/day

Systemic long-term AEL: 0.22 mg/kg bw/day

Method(s) of calculation: Reverse reference method and AEL approach.

Exposure scenario	**Who exposed**	**Exposure/AEL$_{(long\ term)}$ Ratio**
Secondary inhalation exposure to occupants of premises.	Adult	0.004699
	Child	0.007548
	Infant	0.008346
Exposure scenario	**Who exposed**	**Number of gel spots required to reach AEL$_{(short\ term)}$**
Secondary dermal exposure to dislodged or applied gel*	Adult	70
	Child	40.2
	Infant	11.6
Secondary oral exposure to dislodged or applied gel*	Infant	8.8

***Note:** Three secondary exposures are considered using the reverse reference method to calculate the number of spots of Dinotefuran 2 % Bait an individual would have to come into contact with to achieve the systemic AEL. Dinotefuran 2 % Bait will include a bittering agent at 0.01 %.

Because the three secondary exposure scenarios considered using the reverse reference method indicate that contact with, or the consumption of, a relatively low number of spots of Dinotefuran 2 % bait by infants would result in the acute systemic AEL being achieved, it is recommended that the product is labelled with the following phrases:

PREVENT ACCESS TO BAITS by children and animals
KEEP IN A SAFE PLACE

In addition it has been agreed with the Applicant that Dinotefuran 2 % Bait will contain a bittering agent that may discourage ingestion.

Combined exposure

The UK CA considers that none of the primary and secondary exposure scenarios described realistically warrant a combined assessment.

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water	
Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH_4__: >7 d (50 ºC) (equivalent to >1 yr at 12 °C) No degradation products detected
	pH_7__: >7 d (50 ºC) (equivalent to >1 yr at 12 °C) No degradation products detected
	pH_9__: >7 d (50 ºC) (equivalent to >1 yr at 12 °C) No degradation products detected Additional testing performed under extreme alkaline conditions (pH 11 plus pH 13) and elevated temperature demonstrated hydrolysis with formation of UF at both pH. DT_{50} values were 45.0 h (pH 11 and 50 °C) plus 4.2 h (pH 13 and 50 °C).
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	DT_{50} = 1.80 – 7.76 d extrapolated for "seasonal" natural sunlight at 40 °N (or 1.97 – 18.60 d at 50 °N), major metabolites being UF, MG, BCDN and combined DN-2-OH & DN-3-OH (all >10 %), with up to 12 "minor" unidentified products that could not be isolated or identified separately.
Readily biodegradable (yes/no)	No
Biodegradation in seawater	No data provided
Distribution in water / sediment systems (active substance)	Under aerobic conditions at 20 °C, gradual dissipation of dinotefuran reported from water phase to sediment phase then degradation of compound in both river and pond test system. Levels of radioactivity associated with surface water samples declined as incubation progressed, reducing to 48.8 % AR in the river system and 23.4 % AR in the pond system after 56 d. As a result dissipation (water phase) DT_{50} values of 23.0 d at 20 °C for pond system and 49.2 d at 20 °C for river system were proposed. When corrected to 12 °C, dissipation DT_{50} values were predicted as 43.6 d (pond) and 93.3d (river). The radioactivity detected in the sediment phase increased from 0.9 % AR (river system) and 3.8 % AR (pond system) at day 0 to 42.0 % AR (river) and 68.1 % AR (pond) over the same time period (56 d). The major component recovered in the surface water and sediment extracts in all analysed samples up to 7 d after application

	was ^{14}C-labelled dinotefuran (97.2 % AR in river system and 95.2 % AR in pond system as parent). Dinotefuran was shown to degrade slowly but steadily in water-sediment systems with DT_{50} values (at 20 °C) of 59.00 d (total river system) and 46.55 d (total pond system) using sequential "parent & metabolite" SFO kinetic modelling. When corrected to 12 °C, total system degradation DT_{50} values of 88.3 d (pond) and 112 d (river) were predicted.
Distribution in water / sediment systems (metabolites)	Dinotefuran was shown to degrade slowly but steadily in water-sediment systems to form DN as major degradation product. DN reached maximum levels of 23.1 % AR after 180 d (river system) and 32.6 % AR after 103 d (pond system). DT_{50} values (at 20 °C) of 104.9 d (total river system) and 86.8 d (total pond system) using sequential "parent & metabolite" SFO kinetic modelling. When corrected to 12 °C, total system degradation DT_{50} values of 165 d (pond) and 199 d (river) were predicted for DN. 6 other minor degradation products (including UF, MNG and NG) were detected but all were detected at maximum levels of <4 % AR.
Mineralization	Mineralisation occurred gradually over the study until $^{14}CO_2$ reached maximum levels of 19.9 % AR at day 258 (pond system) and 34.9 % AR at day 320 (river system).
Non-extractable residues	Unextracted sediment residues increased steadily over the study, with 62.9 % AR detected in pond system and 28.2 % AR in river system (at 320 d).

Route and rate of degradation in soil	
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (12 °C aerobic): 19.2 d (single soil – silt loam) with r^2 of 0.999 using SFO kinetic modelling
	DT_{90lab} (20 °C, aerobic): 33.9 d (single silt loam soil)
Mineralization (aerobic)	52.1 % AR on day 120 at 20 °C (study completion) Repeat study at 10 °C ran concurrently: 43.7 % mineralisation at day 120
Non-extractable residues	Bound residues accounted for 25.7 % AR at study completion (120 d) Repeat study at 10 °C ran concurrently: 19.9

	% AR associated with bound residues at day 120
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	Principal degradation product was MNG (maximum of 15.6 % AR on day 28), then further degradation reported to NG (maximum of 5.2 % AR on day 62) : 20 °C study. DT_{50lab} for MNG (12 °C aerobic) : 137 d with r^2 of 0.99 (n=1) Repeat study at 10 °C ran concurrently : principal degradation product was MNG (maximum of 16.0 % AR on day 62), then further degradation reported to NG (maximum of 5.4 % AR on day 120).
Field studies (state location, range or median with number of measurements)	DT_{50f}: Not available
	DT_{90f}: Not available
Anaerobic degradation	Anaerobic degradation in flooded soil (silt loam only) incubated under nitrogen at 20 °C. DT_{50lab} (12 °C anaerobic): 146 d (single soil – silt loam) with r^2 of 0.965 using SFO kinetic modelling. DT_{90lab} (20 °C, anaerobic): 256 d (single silt loam soil) Mineralisation : 4.2 % AR on day 120 at 20 °C (study completion) Bound residues accounted for 10.7 % AR on day 59 but decreasing to 9.1 % AR at study completion (120 d) Principal degradation product was DN (maximum of 33.1 % AR on day 120). DT_{50lab} for DN (12 °C aerobic): insufficient degradation to calculate degradation half-life Major metabolite identical to that formed in aerobic water-sediment degradation study so it could be present as a result of flooded soil sample rather than unique anaerobic reactions. However, it is suggested that the process of aeration in water-sediment studies would not disturb sediment layer. Whilst the sediment surface may be aerobic, underlying material would be anoxic and therefore DN can be considered an anaerobic degradate.
Soil photolysis	Not available
Non-extractable residues	None
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	None
Soil accumulation and plateau	None

concentration	
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} : not available

Adsorption/desorption	
Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	K_a 0.119 – 1.221, K_d 1.40 – 9.50. Ka_{oc} 31.4 $L.kg^{-1}$ (arithmetic mean of 5 soil types in advanced test); Kd_{oc} 230.6 $L.kg^{-1}$ (arithmetic mean). No.

Fate and behaviour in air

Direct photolysis in air	DT_{50} = 2.4 h estimated by QSAR
Quantum yield of direct photolysis	Not available
Photo-oxidative degradation in air	Latitude: .N/A.. Season: ...N/A. DT_{50} ..N/A
Volatilization	Not applicable.

Monitoring data, if available	
Soil (indicate location and type of study)	Not available
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: Dinotefuran

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	94 d	NOEC	10.1mg/l
	96 h	LC_{50}	>100 mg/l
Invertebrates			
Chironomus riparius (water spiked study)	27 d	NOEC	2.54 µg/l
	48 h	LC_{50}	72.1 µg/l
Algae			
Pseudokirchneriella subcapitata	96 h	NOE_rC	100 mg/l
	96 h	E_rC_{50}	>100 mg/l
Microorganisms			

Activated sewage sludge respiration inhibition	3 h	NOEC	1000 mg/l
Aquatic plants			
Lemna gibba	7 d	NOEC	110 mg/l
	7 d	EC_{50}	>110 mg/l

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	96 h	LC_{50}	>100 mg/l
Invertebrates			
Chironomus riparius	27 d	NOEC	5 mg/kg
Algae			
Selenastrum capricornutum (now known as Pseudokirchneriella subcapitata)	94 d	E_rC_{50}	>100 mg/l
	94 d	NOEC	100 mg/l
Microorganisms			
Not available			

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

Acute toxicity to ……..	Not available
Reproductive toxicity to *Eisenia fetida*	56 d NOEC 0.2 mg/kg dry soil (0. 0176 mg/kg wet wt)

Effects on soil micro-organisms

Nitrogen transformation & carbon mineralisation	28 d NOEC 4 mg a.s./kg dry soil (3.5 mg a.s./kg wet wt)

Effects on terrestrial vertebrates

Acute toxicity to mammals Acute toxicity to birds Dietary toxicity to birds 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)	0.068 (calculated by QSAR for fish) 0.843 (calculated by QSAR for earthworm)
Depuration time (DT_{50}) (DT_{90}) Level of metabolites (%) in organisms accounting for > 10 % of residues	Not applicable

Chapter 6: Other End Points

None.

Appendix II: List of Intended Uses

Dinotefuran has been evaluated for its intended use as an insecticide (PT 18); data were provided and accepted in support of this intended use.

The product is intended for use by professionals.

Product Type	Insecticide Product Type 18.
Object and/or situation	Indoor use only as a spot or crevice and crack treatment at / near locations where target pests gather.
Product name	Dinotefuran 2 % Bait.
Packaging	Supplied as a ready-to-use syringe style applicator tube.
Categories of User	Professional.
Organisms controlled	Adult and nymph cockroaches (e.g. *B. germanica*).
Formulation type	Gel formulation.
Concentration in formulation	Concentration of dinotefuran is 2.0 % w/w.
Application method/kind	Applied as a spot treatment via syringe.
Application number min/max	Minimum of one application.
Application interval (min)	If necessary, a second application of product should be made after one week (7 days).
Applied amount per treatment	Apply in 0.1 g spots (with each spot containing 0.002 g of dinotefuran). - Apply 0.2 g of product per m^2 for small cockroach species. - Apply 0.4 g of product per m^2 for large cockroach species. - Apply a maximum of 0.8 g of product per m^2 for heavy infestations.
Storage	Store in the closed, original container, in a cool, well ventilated locked place out of reach of children. Do not store in direct sunlight. Dispose of empty container by wrapping in paper, placing in plastic bag and putting in the non-recyclable refuse/waste/garbage.

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

Appendix III: List of Studies

Data protection is claimed by the applicant in accordance with Article 60 of Regulation (EU) No 528/2012 for all study reports marked "Y" in the "Data Protection Claimed" column of the table below. These claims are based on information from the Applicant. It is assumed that the relevant studies are not already protected in any other Member State of the European Union under existing national rules relating to biocidal products. It was however not possible to confirm the accuracy of this information.

Section	Author	Date	Study title	Data Protection claimed	Data Owner
A2. A4-1.1 A4-1.2 **Confidential**	Kumanomido, M.	2005	Analysis of active ingredient and impurities in dinotefuran technical, Japan Analytical Chemistry Consultants Co., Ltd., report no. GT0504, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A2. **Confidential**	Keenan, D.,	2013a	Analysis of [redacted] in six batches of dinotefuran technical. AgChem Product Development, Ricerca Biosciences, LLC. Report no. 030901-1, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A2. **Confidential**	Keenan, D.,	2013b	Method Validation: Analytical method for the determination of [redacted]. AgChem Product Development, Ricerca Biosciences, LLC. Report no. 030900-1, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A2. **Confidential**	Yanagi, M.	2012	Determination of optical rotation of dinotefuran Report no M112010042, non-GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A2.6 A2.8-1 A2.8-2 A2.8-3 A2.8-4 **Confidential**	Anon.	2006	Dinotefuran technical description of starting materials and manufacturing process; dinotefuran technical discussion of formation of impurities, NA Contract Laboratories, no report no., non-GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.1-1 A3.1-2 A3.1-3 A3.1-4 A3.2-1	Malinski M.F.	2000a	MTI-446 Product chemistry, Ricerca, LLC, report no. 011098-1, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.

Section	Author	Date	Study title	Data Protection claimed	Data Owner
A3.4 A3.5-1 A3.6-1 A3.7 A3.9-1 A3.10					
A3.1-1 A3.1-2 A3.1-3 A3.1-4 A3.2-1 A3.4 A3.5-1 A3.6-1 A3.7 A3.9-1 A3.10	Malinski M.F.	2000b	Report amendment: MTI-446 Product chemistry, Ricerca, LLC, report no. 011098-1-1, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.11-1	Tognucci, A.	2001a	Determination of the flammability of MTI-446, RCC Ltd., report no. 780175, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.11-2	Tognucci, A.	2000	Determination of the relative self-ignition temperature of MTI-446, RCC Ltd., report no. 780186, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.13	Tognucci, A.	2001c	Determination of the surface tension of an aqueous solution of MTI-446, RCC Ltd., report no. 780208, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.15	Angly, H.	2001	Determination of the explosive properties MTI-446 according to EC Council Directive 92/69/EEC, Part. A.14, RCC Ltd., report no. 780197, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.16	Tognucci, A.	2001b	Determination of the oxidizing properties (solids) of MTI-446, RCC Ltd., report no. 780210, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.17	Tognucci, A.	2003	Determination of the storage stability and corrosion stability of MTI-446 technical material (shelf life at room temperature), RCC Ltd., report no. 828865, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.2-1	Labano, S.	2012	Expert statement. Dinotefuran:	Y	Mitsui

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			calculation of Henry's Law Constant, LKC Switzerland Ltd., report no. 11-LKC-04, non-GLP, unpublished		Chemicals Agro, Inc.
A3.2-2 A3.5-2 A3.6-2 A3.9-2	Sydney, P.	1996	MTI-446: Determination of the physico-chemical properties, Huntington Life Sciences, report no. MTO097/980159, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.3-1	Shimono S.	1999a	Physical state of dinotefuran (MTI-446), Mitsui Chemicals, Inc. Life Science Laboratory, no report no., non-GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.3-2	Shimono S.	1999b	Colour of dinotefuran (MTI-446), Mitsui Chemicals, Inc. Life Science Laboratory, no report no., non-GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A3.3-3	Shimono S.	1999c	Odour of dinotefuran (MTI-446), Mitsui Chemicals, Inc. Life Science Laboratory, no report no., non-GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A4.2(a)	MacGregor, J.A., Van Hoven, R.L., Nixon, W. B.	2002	Independent laboratory validation of methods for the analysis of MTI-446 and its metabolite MNG in soil, Wildlife International, Ltd., report no. 236C-106, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A4.2(a)	Wais, A.	2001	Validation of the residue analytical method for MTI-446 in soil, RCC Ltd., report no. 739923, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A4.2(c)	Schreitmüller, J.	2002a	Development and validation of a residue analytical method for MTI-446 in drinking, ground and surface water, RCC Ltd., report no. 841987, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A4.2(c)	Schreitmüller, J.	2002b	First amendment to report: Development and validation of a residue analytical method for MTI-446 in drinking, ground and surface water, RCC Ltd., report no. 841987, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A5.2.1	Heaven, H.	2011	Laboratory bioassay to	Y	Mitsui

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			determine the efficacy of dinotefuran technical against German cockroaches (*Blattella germanica*) and houseflies (*Musca domestica*). i2L Research Ltd, Report No. 11/07 (unpublished).		Chemicals Agro, Inc.
A6.1.1-1	[redacted]	1997a	Acute oral toxicity study of MTI-446 in rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.1.1-2	[redacted]	1997b	Acute oral toxicity study of MTI-446 in mice [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.1.1-2	[redacted]	2000	First amendment to report - Acute oral toxicity study of MTI-446 in mice [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.1.2	[redacted]	1997c	Acute dermal toxicity study of MTI-446 in rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.1.3	[redacted]	1999	MTI-446: Acute inhalation (nose only) toxicity study in the rat [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.1.3	[redacted]	2000a	First amendment to report - MTI-446: Acute inhalation (nose only) toxicity study in the rat [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.1.3	[redacted]	2000b	Second amendment to report -	Y	Mitsui

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			MTI-446: Acute inhalation (nose only) toxicity study in the rat [redacted] GLP, unpublished		Chemicals Agro, Inc.
A6.1.4.d	[redacted]	1998a	Primary dermal irritation study of MTI-446 in rabbits [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.1.4.e	[redacted]	1998b	Primary eye irritation study of MTI-446 in rabbits [redacted] unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.1.5	[redacted]	1997d	Dermal sensitization study of MTI-446 in guinea pigs - maximisation test [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.10-1	[redacted]	2011	Dinotefuran: 4-week dietary immunotoxicity study in the CD rat [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.10-2	[redacted]	2011	Dinotefuran: 4-week dietary immunotoxicity study in the CD-1 mouse [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.2-1	[redacted]	2000a	Metabolism of [^{14}C]-MTI-446 in rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.2-1	[redacted]	2000b	First amendment to report – Metabolism of [^{14}C]-MTI-446 in	Y	Mitsui Chemicals

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			rats [redacted] GLP, unpublished		Agro, Inc.
A6.2-1	[redacted]	2001	Second amendment to report – Metabolism of [^{14}C]-MTI-446 in rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.2-2	[redacted]	2000c	Absorption, distribution, metabolism and excretion of [G-^{14}C]-MTI-446 following administration of a single oral dose to neonatal rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.2-2	[redacted]	2000d	First amendment to report - Absorption, distribution, metabolism and excretion of [G-^{14}C]-MTI-446 following administration of a single oral dose to neonatal rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.2-3	[redacted]	2006b	Dermal absorption of [^{14}C]MTI-446 formulated as aqueous solution in the rat (in vivo) [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.3.1-1	[redacted]	1997a	4-week dietary toxicity study with MTI-446 in rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.3.1-2	[redacted]	1997b	4-week dietary toxicity study with MTI-446 in mice [redacted]	Y	Mitsui Chemicals Agro, Inc.

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			[redacted] GLP, unpublished		
A6.3.2	[redacted]	2001b	28-day dermal toxicity study with MTI-446 in rat [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.3.3	[redacted]	2002	MTI-446: 28-day inhalation (nose only) toxicity study in the rat [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.4.1-1	[redacted]	1997c	13-week dietary toxicity study with MTI-446 in rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc
A6.4.1-1	[redacted]	2000a	First amendment to report - 13-week dietary toxicity study with MTI-446 in rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc
A6.4.1-2	[redacted]	1997d	13-week dietary toxicity study with MTI-446 in mice [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc
A6.4.1-2	[redacted]	2000b	First amendment to report: - 13-week dietary toxicity study with MTI-446 in mice [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc
A6.4.1-3	[redacted]	1999a	13-week dietary toxicity study with MTI-446 in dogs [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc
A6.4.1-3	[redacted]	1999b	First amendment to report - 13-	Y	Mitsui

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			week dietary toxicity study with MTI-446 in dogs [redacted] GLP, unpublished		Chemicals Agro, Inc
A6.5-2	[redacted]	1999c	52-week dietary chronic toxicity study with MTI-446 in dogs [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc
A6.5-2	[redacted]	2005	Historical control data for 52-week dog studies [redacted] unpublished	Y	Mitsui Chemicals Agro, Inc
A6.6.1-1	[redacted]	1996	MTI-446: Microbial reverse mutation assay [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc
A6.6.1-2	[redacted]	1999	A DNA repair assay of *Bacillus subtilis* on MTI-446 [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc
A6.6.1-3	[redacted]	1996	MTI-446: *In vitro* mammalian cytogenetics test [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc
A6.6.1-4	[redacted]	2002	MTI-446 technical material: mutation at the thymidine kinase (tk) locus of mouse lymphoma L5178Y cells (MLA) using the microtitre fluctuation technique [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc
A6.6.4	[redacted]	1995	Micronucleus test of EXP-316 with mice	Y	Mitsui Chemicals

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			[redacted] GLP, unpublished		Agro, Inc.
A6.7-1, Cross ref. A6.5-1	[redacted]	2000c	104-week dietary combined chronic toxicity and carcinogenicity study with MTI-446 in rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.7-2	[redacted]	2000d	78-week dietary carcinogenicity study with MTI-446 in mice [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.7-2	[redacted]	2000e	First amendment to report - 78-week dietary carcinogenicity study with MTI-446 in mice [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.8.1-1	[redacted]	1998b	Teratogenicity study of MTI-446 given orally to rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.8.1-2	[redacted]	1998e	Teratogenicity study of MTI-446 given orally to rabbits [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.8.2-1	[redacted]	2001	MTI-446 technical preliminary two generation study in the Han Wistar rat [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.8.2-2	[redacted]	2002	MTI-446 two-generation reproduction study in the Han Wistar rat by oral (dietary) administration	Y	Mitsui Chemicals Agro, Inc.

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			[redacted] GLP, unpublished		
A6.9-1	[redacted]	2001a	Acute oral gavage neurotoxicity study with MTI-446 in rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.9-2	[redacted]	2001b	13-week dietary neurotoxicity study with MTI-446 in rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.9-3	[redacted]	2006a	Transfer of [^{14}C]MTI-446 into milk of lactating rats after oral administration [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.9-4	[redacted]	2009	Oral (Diet) Dosage-range finding developmental neurotoxicity and immunotoxicity study of MTI-446 (Dinotefuran) in Crl:CD (SD) rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A6.9-5	[redacted]	2010	Oral (Diet) developmental neurotoxicity study of MTI-446 (Dinotefuran) in Crl:CD (SD) rats [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.1.1.1.1	Sydney, P.	1998 & 2000	MTI-446 : Determination of hydrolysis as a function of pH, Huntingdon Life Sciences, , report no. 95/MTO098/1216 (MRID 45640101). (GLP, unpublished) &	Y	Mitsui Chemicals Agro, Inc.

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			Report amendment 1 : Determination of hydrolysis as a function of pH, Huntingdon Life Sciences, , report no. 95/MTO098/1216. (Unpublished)		
A7.1.1.1.2	Van der Gaauw, A.	2002	Aqueous Photolysis of ^{14}C-MTI-446 under Laboratory Conditions and Determination of Quantum Yield, RCC Ltd., report no. 729011 (MRID 45640105). (GLP, unpublished)	Y	Mitsui Chemicals Agro, Inc.
A7.1.1.2.1	Feil-Klein, N.	2012	Ready biodegradability of dinotefuran technical in a manometric respirometry test, IBACON, report no. 70891163. (GLP, unpublished)	Y	Mitsui Chemicals Agro, Inc.
A7.1.2.2.2	Völkel, W.	2000	^{14}C-MTI-446 : Degradation and Metabolism in Aquatic Systems, RCC Ltd., report no. 709604. (GLP, unpublished)	Y	Mitsui Chemicals Agro, Inc.
A7.1.3	Völkel, W.	2001	Adsorption/desorption of ^{14}C-MTI-446 on soils, RCC, Ltd., report no. 728998. (GLP, unpublished)	Y	Mitsui Chemicals Agro, Inc.
A7.2.1-1	Völkl, S.	2003a	^{14}C-MTI-446 : Metabolism in one soil incubated under aerobic conditions, RCC Ltd., report no. 843175. (GLP, unpublished)	Y	Mitsui Chemicals Agro, Inc.
A7.2.1-2	Völkl, S.	2003b	^{14}C-MTI-446 : Anaerobic soil degradation and metabolism, RCC Ltd., report no. 841703. (GLP, unpublished)	Y	Mitsui Chemicals Agro, Inc.
A7.3.1	Van der Gaauw, A.	2000	Estimation of the degradation of MTI-446 by photo-oxidation in air, RCC, Ltd., report no. 731160 (MRID 45640110). (QSAR, unpublished)	Y	Mitsui Chemicals Agro, Inc.
A7.4.1.1-1	[redacted]	1999	Acute toxicity of MTI-446 to Rainbow trout (*Oncorhynchus mykiss*) in a 96-Hour static test [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.1.1-1	[redacted]	2000a	First amendment to report:	Y	Mitsui

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			acute toxicity of MTI-446 to Rainbow trout (*Oncorhynchus mykiss*) in a 96-Hour Static Test [redacted] GLP, unpublished		Chemicals Agro, Inc.
A7.4.1.1-2	[redacted]	2002a	DN phosphate determination of acute toxicity to Rainbow trout (96 h, Semi-static) [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.1.2-1	Peither, A.	2000b	Acute toxicity of MTI-446 to *Daphnia magna* in a 48-hour immobilization test, RCC Ltd., report no. 740968, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.1.2-1	Peither, A.	2000c	First Amendment to Report: Acute Toxicity of MTI-446 to *Daphnia magna* in a 48-Hour Immobilization Test, RCC Ltd., report no. 740968, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.1.2-2	Kelly, C.R., Murphy, C.M., Allan, J.	2001	DN phosphate determination of acute toxicity to *Daphnia* (48 h, Static), Inveresk Research, report no. 20122, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.1.3-1	Seyfried, B.	2000a	Toxicity of MTI-446 to *Pseudokirchneriella subcapitata* (formerly *Selenastrum capricornutum*) in a 96-hour algal growth inhibition test, RCC Ltd., report no. 740981, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.1.3-1	Seyfried, B.	2000b	First amendment to report: Toxicity of MTI-446 to *Pseudokirchneriella subcapitata* (formerly *Selenastrum capricornutum*) in a 96-hour algal growth inhibition test, RCC Ltd., report no. 740981, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.1.3-1	Seyfried, B.	2000c	Second amendment to report: Toxicity of MTI-446 to	Y	Mitsui Chemicals

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			Pseudokirchneriella subcapitata (formerly *Selenastrum capricornutum*) in a 96-hour algal growth inhibition test, RCC Ltd., report no. 740981, GLP, unpublished		Agro, Inc.
A7.4.1.3-2	Kelly, C.R., Ferguson, K.	2002b	DN phosphate alga, growth inhibition test (96 h), Inveresk Research, report no. 19849, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.1.4	Falk, S.	2012	Toxicity testing of dinotefuran technical- on microorganisms with the activated sludge respiration inhibition test, Eurofins Agroscience Services, report no. S11-03209, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.3.2	[redacted]	2001	Toxic effects of MTI-446 to Rainbow trout (*Oncorhynchus mykiss*) in an early-life stage toxicity test [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.3.4	Peither, A.	2000d	Influence of MTI-446 on survival and reproduction of *Daphnia magna* in a semistatic test over three weeks, RCC Ltd, report no. 752106, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.3.5.1-1	Memmert, U.	2000	Acute toxicity of MTI-446 to first-instar larvae of *Chironomus riparius*, RCC Ltd., report no. 752128, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.3.5.1-2	Memmert, U.	2003	Effects of MTI-446 on the development of sediment-dwelling larvae of *Chironomus riparius* in a water sediment system, RCC Ltd., report no. 844569, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.4.3.5.1-3	Memmert, U.	2007	Effects of DN phosphate on the development of sediment-dwelling larvae of *Chironomus riparius* in a water-sediment system with spiked sediment, RCC Ltd, report no. 844571,	Y	Mitsui Chemicals Agro, Inc.

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			GLP unpublished		
A7.4.3.5.2	Bätscher R.	2002	Toxicity of MTI-446 to the aquatic higher plant *Lemna gibba* in a 7-day semistatic growth inhibition test, RCC Ltd., report no. 827752, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.5.1.1	Völkel, D.	2000	The effects of MTI-446 20% SG on soil respiration and nitrification, RCC Ltd, 747281, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
A7.5.2.1	Bätscher, R.	2001	Effects of MTI-446 on survival, growth and reproduction of the earthworm *Eisenia fetida*, RCC Ltd, report no. 731193, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
B2.2	Anonymous	2011	MSDS of Roachdown Gel, Mitsui Chemicals Agro, Inc., Shiodome City Center 1-5-2, Higashi-Shimbashi, Minato-ku Tokyo 105-7117, Japan, non-GLP, published.	N	-
B3.1-1 B.3.1-2 B.3.5	Takahashi, N., Shiraki, A. and Tobinaga, M.	2010a	Pest control bait product "New GOK1": data on setting of specifications and test methods, Experiment Building, Research & Development Dept., Osaka Kasei, Co., Ltd., 2-6-11, Nakashima, Nishiyodogawa-ku Ward, Osaka City, Osaka 555-0041, Japan, no report no., non-GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
B3.2	Cage, S.	2012a	Dinotefuran 2 % bait explosive properties, Huntington Life Sciences Ltd., Report No. MCW0034, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
B3.3	Cage, S.	2012b	Dinotefuran 2 % bait oxidising properties, Huntington Life Sciences Ltd., report no. MCW0036, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
B3.7 B3.10-2	Takahashi, N., Shiraki, A. and Tobinaga, M.	2010b	Pest control bait product "New GOK1" stability data, Experiment Building, Research & Development Dept., Osaka Kasei, Co., Ltd., 2-6-11, Nakashima, Nishiyodogawa-ku, Osaka City, Osaka 555-0041, Japan, no report no., non-GLP,	Y	Mitsui Chemicals Agro, Inc.

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			unpublished		
B4.1	Cage, S.	2012c	Dinotefuran 2 % bait: method validation, Huntington Life Sciences Ltd., report no. MCW0035, GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.1.1-1	[redacted]	2010a	Acute oral toxicity of New GOK1 to the rat - limit test [redacted] GLP; unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.1.1-1	[redacted]	2010b	Amendment to Final Report - Acute oral toxicity of New GOK1 to the rat - limit test [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.1.1-2	[redacted]	2010c	Acute oral toxicity of New GOK1 to the mouse - limit test [redacted] GLP; unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.1.1-2	[redacted]	2010d	Amendment to final report - acute oral toxicity of New GOK1 to the mouse - limit test [redacted] GLP; unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.1.2-1	[redacted]	2009a	Acute dermal toxicity test with New GOK1 in the rat - limit test [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.1.2-1	[redacted]	2010e	Amendment to final report - Acute dermal toxicity test with New GOK1 in the rat - limit test [redacted] GLP, unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.1.2-2	[redacted]	2009b	Acute dermal toxicity test with New GOK1 in the mouse - limit test [redacted]	Y	Mitsui Chemicals Agro, Inc.

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			[redacted] GLP; unpublished		
B6.1.2-2	[redacted]	2010f	Amendment to Final Report - Acute Dermal Toxicity Test with New GOK1 in the Mouse - Limit Test [redacted] GLP; unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.2.d	[redacted]	2010a	Acute dermal irritation/corrosion test (patch test) of New GOK 1 in rabbits [redacted] GLP; unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.2.e	[redacted]	2010b	Acute eye irritation/corrosion test of New GOK 1 in rabbits [redacted] GLP; unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.3	[redacted]	2010a	Skin sensitisation test of New GOK 1 in guinea pigs-according to the E.V. Buehler method [redacted] GLP; unpublished	Y	Mitsui Chemicals Agro, Inc.
B6.3	[redacted]	2010b	Amendment No.1 to final report - Skin sensitisation test of New GOK 1 in guinea pigs-according to the E.V. Buehler method [redacted] GLP; unpublished	Y	Mitsui Chemicals Agro, Inc.
IIB 3.2	Joint Research Council	June 2002	Technical Notes for Guidance on Human Exposure to Biocidal Products. Published.	N	Public domain
IIB 3.2	ExpoFacts	2001	Exposure factors sourcebook for European populations. European centre for ecotoxicology and toxicology of chemicals, Brussels, Belgium.	N	Public domain

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			Technical report No 79. Published.		
IIB 3.2	European Chemicals Bureau	2003	Part 1 – Technical Document On Risk assessment in support of Directive 93/67/EEC (risk assessment for new notified substances); EC Regulation No. 1488/94 (Risk assessment for Existing Substances); and Directive 98/8/EC (concerning the placing of biocidal products on the market). European Chemicals Bureau. Published.	N	Public domain
IIB 3.2	Joint Research Council	Sept 2011	Default protection factors for protective clothing and gloves. HEEG opinion agreed at TM I 2010. Manual of Technical Agreements of the Biocides Technical Meeting (MOTA), Version 4, section 4.2.9.9, p29.	N	Public domain
IIIB 5.10.2-1	Koizumi, T.	2010	Dinotefuran bait product: field efficacy study against German cockroach. Japan Environmental Sanitation Center, East Branch Office, Environmental Biology Dept, Report No. 18-EB-911-035 (unpublished).	Y	Mitsui Chemicals Agro, Inc.
IIIB 5.10.2-2	Kosone, K.	2010	Field efficacy study against German cockroach. Yokohama City Institute of Health (unpublished).	Y	Mitsui Chemicals Agro, Inc.
IIIB 5.10.2-3	Kazuma, T.	2010	Dinotefuran bait product and reference product: *ad libitum* feeding study against German cockroach. Japan Environment Sanitation Center, East Branch Office, Environmental Biology Dept, Report No. 18-EB-911-033 (unpublished).	Y	Mitsui Chemicals Agro, Inc.
IIIB 5.10.2-4	Kazuma, T. and Minagawa, K.	2010	Dinotefuran bait product and reference product: *ad libitum* feeding study against German cockroach (strain that shows dietary aversion to sucrose). Japan Environment Sanitation	Y	Mitsui Chemicals Agro, Inc.

Section	Author	Date	Study title	Data Protection claimed	Data Owner
			Center, East Branch Office, Environmental Biology Dept, Report No. 18-EB-911-034 (unpublished).		
IIIB 5.10.2-5	Nagai, J.	2010	Dinotefuran bait product: *ad libitum* feeding study against German cockroach. Mitsui Chemicals Agro, Inc (unpublished).	Y	Mitsui Chemicals Agro, Inc.
IIIB 5.10.2-6	Kazuma, T. and Minagawa, K.	2010	Dinotefuran bait product and reference product: *ad libitum* feeding study against Smokybrown cockroaches. Japan Environment Sanitation Center, East Branch Office, Environmental Biology Dept, Report No. 18-EB-911-032 (unpublished).	Y	Mitsui Chemicals Agro, Inc.