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

Evaluation of active substances

Assessment Report

HEXAFLUMURON

Product-type 18
(Insecticide)

February 2015

Portugal

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Principle of evaluation

This assessment report has been established as a result of the evaluation of Hexaflumuron as product-type 18 (insecticides), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with the original view to the possible inclusion of this substance into Annex I or IA to that Directive.
The evaluation has therefore been conducted in the view to determine whether it may be expected, in light of the common principles laid down in Annex VI to Directive 98/8/EC, that there are products in product-type 18 containing Hexaflumuron that will fulfill the requirements laid down in Article 5(1) b), c) and d) of that Directive.

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 Hexaflumuron 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. Procedure followed

This assessment report has been established as a result of the evaluation of the active Hexaflumuron as product-type 18 (Insecticide), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market.

Hexaflumuron (CAS no. 86479-06-3) was notified as an existing active substance, by Dow AgroSciences S.A., hereafter referred to as the applicant, in product-type **18**.

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

[1] Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1
[2] Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council

In accordance with the provisions of Article 7(1) of that Regulation, Portugal was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for Hexaflumuron as an active substance in Product Type 18 was no earlier than 1 November 2005 and no later than 30 April 2006, in accordance with Part B of Annex V of Regulation (EC) n.º 2032/2003.

On 26 April 2006, Portugal competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 31 July 2006.

On 18 July 2011, the Rapporteur Member State submitted, in accordance with the provisions of Article 14(4) and (6) of Regulation (EC) No 1451/2007, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 5 September 2011. The competent authority report included a recommendation for the inclusion of Hexaflumuron in Annex I to the Directive for PT 18.

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 technical and competent authority meetings, at the Biocidal Products Committee and its Working Groups meetings and the competent authority report was amended accordingly.

In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalized during its meeting held on [date].

concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

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

Hexaflumuron is a white odourless powder at room temperature. It is denser than water and undergoes no thermal decomposition below its melting temperature, which is in the region of 200°C. It decomposes below its boiling point. It was shown not to be technically feasible to accurately determine the dissociation constant due to the fact that the molecule does not contain reversible ionisable functional groups. Its vapour pressure is very low and hence its Henry's Law Constant indicates that volatilisation is not expected to significantly contribute to the dissipation of Hexaflumuron in the environment. Hexaflumuron is soluble in polar and non polar organic solvents. Hexaflumuron is not considered to possess explosive or oxidizing properties.
The methods of analysis for the active substance as manufactured and for the determination of impurities have been validated. The methods of analysis in environmental matrices, as appropriate for the areas of use assessed, have been validated and shown to be sufficiently sensitive with respect to the levels of concern. The method for quantitative determination of residues of Hexaflumuron in ground, surface, drinking and flooded bait water has a validated LoQ of 0.001 µg/L (IIIA 4.2, Ref. O40). The sediment and soil method for Hexaflumuron has a validated LoQ of 0.010 µg/g (IIIA 4.2, Ref. O38).

2.1.2. Intended Uses and Efficacy

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against *Reticulitermes* species, *Coptotermes* species, and *Heterotemes* species 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.
Hexaflumuron is used in products for insect control (Main Group 03, Product type 18, insecticides).
Hexaflumuron is used to control: *Reticulitermes* species, *Coptotermes* species, and *Heterotemes.*
In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.3. Classification and Labelling

Proposed classification and labelling based on Directive 67/548/EEC:

Classification	N; R50/53	
Hazard symbol	N	
Class of danger	N - Dangerous for the environment	
R-phrases	R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment	

S-phrases	S2 – Keep out of reach of children S60- This material and its container must be disposed of as hazardous waste S61 – Avoid release to the environment. Refer to special instructions/safety data sheets
Specific Concentration Limits	N; R50-53: C ≥ 0.025% N; R51-53: 0.0025% ≤ C < 0.025% R52-53: 0.00025% ≤ C < 0.0025%

Proposed classification and labelling based on CLP Regulation, under evaluation in the RAC:

CLASSIFICATION		
Hazard Class and Category	Acute Aquatic Category 1 Chronic Aquatic Category 1	
H-Statements	H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects	
LABELLING		
Pictogram	GHS09	
Signal Word	Warning	
H-Statements	H410: Very toxic to aquatic life with long lasting effects	
M-factors	Acute M-factor = 1 000 Chronic M-factor = 10 000	

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

The product, RECRUTE Pro contains 0.5% w/w hexaflumuron for application by professional trained operators.

In line with the TNsG on Human Exposure to Biocidal Products, the PT CA has carried out for this product (RECRUTE Pro) and its specified uses an exposure assessment for human health based on a tiered approach and using worst-case assumptions when applicable and realistic. If the risks to human health following exposure to hexaflumuron were considered to be acceptable following comparison of the predicted systemic dose with the appropriate NOAEL from animal studies, then no further refinement of the exposure scenario was carried out.

The risk characterisation follows the principles agreed by the Biocides Technical Meeting, described in Technical Guidance Documents for Risk Characterisation of Systemic Effects[3]. The risk characterisation for systemic effects is conducted by comparison of the exposure and the toxicity by both the margin of exposure (MOE) approach and the Acceptable

[3] http://ec.europa.eu/environment/biocides/pdf/tnsg_4_1.pdf

Exposure Limit (AEL) approach for systemic toxicity. The MOE is calculated as: MOE = N(L)OAEL (mg/kg bw/day) /Exposure (mg/kg bw/day) and this is then compared to the acceptable minimal MOE that has been derived. In the AEL concept the exposure estimates are compared with the determined systemic AEL = N(L)OAEL (mg/kg bw/day)/overall Assessment Factor (AF). Risk are considered acceptable if the calculated MOE is > minimal.

2.2.1.1. Hazard identification & Effects assessment

The toxicity of hexaflumuron has been investigated in studies in laboratory animals. The majority of studies were conducted to GLP and guideline compliant. Where deviations existed, the studies were still considered to be of an acceptable standard. Overall, there is no concern over the quality of the data submitted.

The endpoints addressed by studies conducted with hexaflumuron (XRD 473) are toxicokinetics, acute toxicity, irritation and corrosivity, sensitisation, sub-acute, sub-chronic and chronic toxicity, carcinogenicity, genotoxicity (in vitro, in vivo), reproductive toxicity (teratogenicity, fertility) and neurotoxicity.

The potential toxicity of RECRUTE Pro was assessed by means of acute testing (acute oral, dermal and skin and eye irritation, skin sensitisation) conducted with Recruit 50%, a liquid suspension of hexaflumuron that corresponds to the Manufacturing Use Concentrate (MUC). There is only one co-formulant (Proxel GXL) that contains a substance listed under 67/548/EEC (1,2-benzisothiazol-3(2H)-one (CAS 2634-33-5) at up to 20%. However, the total concentration of this co-formulant in the MUC and in the finished bait is not associated with any of the hazards noted for the individual constituent. This has been demonstrated by acute testing (i.e., skin, eye irritation, skin sensitization) for the MUC with all negative results and didn't trigger any hazard classification.

The toxicokinetic studies showed that following single oral doses, hexaflumuron is well-absorbed in the rat following oral administration at low (5 mg/kg bw) dose levels, but saturation at higher (250 mg/kg bw) dose levels resulting in substantially less absorption. Oral (gavage) exposure of 5 mg/kg bw in rats and mice result in absorptions higher than 80% and 90% respectively.

Peak plasma levels occur from 4-8 hours following exposure attesting to the rapid and significant degree of absorption at lower dose levels. Distribution of hexaflumuron is characterized as moderate with recoveries seen predominantly in liver>kidney>fat. Elimination after oral administration occurs through both urinary and fecal excretion with half-lives ranging from 14-30 hours depending on the radiolabelled material. Elimination of hexaflumuron in the blood appears to be associated with the plasma, with no evidence of accumulation in the blood cells. Metabolism of hexaflumuron appears to be extensive with little parent compound detected following exposure. Identified metabolites include 2,6-difluorobenzoic acid and 2,6-difluorobenzamide, along with 3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)aniline and 1-(3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenyl)urea.

Given the saturation of absorption at higher dose levels, coupled with the extensive metabolism and excretion profile for hexaflumuron, mammalian bioaccumulation is not expected to occur.

There is no direct measure of dermal penetration for hexaflumuron. A conservative estimation of 12.5% dermal penetration was established based on the 3-week rat dermal study and 13-week rat oral study. This estimate is acceptable for simple mixtures, but needs to be further assessed when the active substance is used in complex mixtures, since co-presence of other chemicals (solvents, surfactants etc.) can impact the dermal absorption of the active substance.

There is no direct measure of inhalation absorption for hexaflumuron. Therefore, a "worst case" default of 100% absorption following inhalation exposure is proposed for use in the risk assessment.

Hexaflumuron has been evaluated in a series of toxicity studies of varying duration aimed at characterizing its hazard potential. Hexaflumuron is of low acute toxicity by oral and inhalation route with a LD50 exceeding 5000 mg/kg bw and LC50 exceeding 7 mg/L. Dermal studies show low toxicity with LD50 exceeding 2000 mg/kg bw/d. In addition, it is not an eye or skin irritant nor a skin sensitizer according to the study results. Hence, Hexaflumuron does not meet the criteria for the classification for these hazards.

Repeated exposure to hexaflumuron has been investigated by the oral route in subacute studies (rats, mice, and dogs), in subchronic studies (mice and rats) and in chronic studies (rats and dogs). Increased methemoglobin (MetHb) was the major finding in all studies and considered as the critical adverse effect for the risk assessment and NOAEL setting. The lowest relevant NOAEL (used to set the long-term AEL) was 0.5 mg/kg bw/day based on an increase in methemoglobin and an increase in hepatic hemosiderin deposits from the 52-week dog study.

Hexaflumuron was negative for tumourigenicity as evaluated in carcinogenicity studies in both mice and rats.

The genotoxic potential of hexaflumuron was investigated in three in vitro and one in vivo assay. Results of these tests indicate that hexaflumuron is devoid of any genotoxic potential in prokaryotic and eukaryotic cells.

The hexaflumuron 2-generation rat study presented indicated that the reproductive NOAEL is 125 mg/kg bw, and the NOAEL for paternal hematopoietic toxicity is 5 mg/kg bw. However, this test was conducted prior to the OECD 416 guideline was adopted, hence sensitive reproductive parameters like oestrus cycle, and sperm parameters were not assessed. It is concluded that reproductive toxicity is not the critical toxic endpoint, since the lowest NOAEL of 5 mg/kg bw/d for paternal toxicity is above the repeated dose NOAEL used for risk assessment (see section 3.5).

Hexaflumuron was tested with negative results in an acute delayed neurotoxicity study in the domestic hen. Therefore, hexaflumuron is not considered a neurotoxicant.

2.2.1.2. Exposure assessment

The manufacture of hexaflumuron is done in the European Union under contract for the Applicant and is shipped to USA to be formulated into the Manufacturing Use Concentrate (MUC 50 % hexaflumuron, EF-1104). This concentrate is applied onto alpha cellulosic briquettes and are packed either in sachets for the above ground station or in bait tubes for the below ground station. The formulation and production of the bait station is also done in the USA, according to national occupational safety and health regulations. Subsequently, the biocidal product is imported into the EU for placing in the market and is to be used by professional users only.

Professional users

Exposure to Production / formulation of active substance

Hexaflumuron production in the EU is planned for less than 3 weeks every year, due to the low quantity needed to be incorporated in the biocidal product RECRUTE Pro.

Inhalation exposure: Employees are trained with working with irritating or even toxic gases or liquids and with wearing gas- and dust-masks. Safety measures according to the manufactured material are put in place and clearly stated in an accompanying report. Exposure via inhalation during manufacture is controlled by filter systems, ventilation systems, masks and measuring devices and therefore inhalation exposure is considered to be extremely low.

Dermal exposure: Dermal exposure is usually not measured but considered to be negligible as the employees are wearing adequate personal protective equipment (PPE).

The exposure during the formulation of the biocidal product is not assessed by the PT CA under the requirements of the BPD. However, the PT CA assumes that the production is performed in conformity with national and European occupational safety and health regulations.

Exposure to the Representative Product when handled

The potential exposure of operators was determined using the German Model Database for Mix/Load (BBA 1992) that contains data for mixing/loading solid formulations. The scenarios considered in the TNsG - Human Exposure to Biocidal Products, as revised by User Guidance version 1 (EC, 2002) are not adequate to assess the unique way that hexaflumuron is used, as a termicide.

Exposure assessment was conducted based on the use of the product, RECRUTE Pro (also designated GF-1407). This product is a 100g solid bait (briquettes enclosed in plastic bag) containing 0.5% hexaflumuron. During the installation phase, the pest controller injects 200 ml of water into the bag and re-seals the bag. The resulting mixture is a dough like bait which is enclosed within the plastic bag. The bait (in bag) is placed into the bait station.

The mixing/loading component with a formulation "WG" (water dispensable granules) using 75th percentile values were considered relevant for this use pattern. The systemic dose from the total of dermal and inhalation exposures for hexaflumuron have been calculated assuming an operator body weight of 60 kg, a dermal penetration of 12.5% and inhalation absorption of 100%.

The relevant scenario used for exposure assessment is "Professionals who handle and dispose of the product (installation, inspection and de-installation of in-ground and above ground stations).

For Tier 1 exposure assessment, a conservative daily exposure was estimated assuming that an operator can install 24 stations in one day, or inspect 50 stations in one day or de-install 40 stations per day. It was also assumed that gloves were worn because they are required to avoid any potential contact with the bait and that they offer 90% protection.

Three activities were identified: installation, inspection and de-installation of the bait stations (in-ground and above ground). For the installation, a dermal uptake of 4.2E-04 mg/kg bw/day and a inhalation uptake of 1.2E-05 mg/kg bw/day (4.4E-04 mg/kg bw/day total uptake) were estimated. For the inspection and de-installation tasks, values for inhalation and dermal uptakes were respectively, 2.5E-05, 8.9E-04 (9.1-04 mg/kg bw/day total uptake) and 2.0E-05, 7.1E-04 mg/kg bw/day (7.3E-04 mg/kg bw/day total uptake).

As the exposure pattern can include short, medium and long-term events, the PT CA considered relevant for use in the risk characterization the NOAEL/Acceptable Exposure Limits (AEL) for short, medium and long-term durations.

Non-Professional users

RECRUTE Pro bait stations are only available to the professional pest controller.

Secondary Exposure

RECRUTE Pro is used inside a plastic bag, which is inside an enclosed bait station. Secondary exposure to professionals is not expected to occur during normal use of the product. However, if the station breaks and releases the bait, humans can come into contact with the bait. The following potential secondary exposure scenarios were considered possible:

1. Short-term dermal exposure to infant, child or adult that comes into contact with the bait.

2. Short-term oral exposure to infant by mouthing of poison bait.

3. Short-term oral exposure to infant ingestion of unsecured bait.

Dermal exposure (scenario 1) - a reverse reference scenario was used for Tier 1 assessmentfor short-term dermal exposure to infant, child or adult that come into contact with the bait (see doc IIB for calculations). However, since the above ground station containing the product consists of a rigid plastic housing containing the bait matrix package and this tamper resistant closed bait station is fixed by screws and glued to the wall, such an exposure is unlikely to occur and the risk is considered mitigated.

The scenario used to assess infant acute exposure by mouthing of poisoning bait was similar to that used in rodenticides (PT14) bait box scenario listed in the TNsG, part 3, Appendix 7.2.1. Similarly to the dermal exposure, mouthing and accidental ingestion is unlikely to occur due to the design of the bait station and therefore risks are considered mitigated. Nonetheless, it is recommended to label the product with "Keep out of reach of children".

2.2.1.3. Risk characterisation

The relevant scenario for risk characterisation of hexaflumuron used in the representative product RECRUTE Pro bait system (PT18) is the handling and disposing of the product (installation, inspection and de-installation of in-ground and above ground stations).

Furthermore, the secondary exposure scenarios specifically in case of bait station damage were also used in the risk characterisation. These scenarios consist of the infant into dermal contact with bait, the infant by mouthing of poison bait and the infant mouthing of unsecured bait and ingesting.

For risk characterisation, the total internal body burden resulting from the relevant exposure scenarios is compared to the short-term, medium-term and long-term AELs, 0.08, 0.005 and 0.005 mg/kg bw/day, respectively. The AELs (as internal reference values) are based upon the oral short-, medium-, and long-term NOAELs of 8.3, 0.5 and 0.5 mg/kg/d, respectively. Risks are considered acceptable if the MOE is > 100 or if the systemic exposure/AEL ratio is < 1.

Risk characterisation results are tabulated in section 2.3.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Biodegradation

Hexaflumuron cannot be considered to be readily biodegradable and should be considered as persistent, having an aerobic soil metabolism half-life of approximately 280 days. The core aerobic soil studies were conducted at 25°C and were reanalyzed per latest FOCUS Kinetics guidance and recalculated using 0-120 day data only rather than 0-365 days according to OECD 307 study guidance (range 94 – 129 days (arithmean = 100 days, geomean = 99 days)). One test conducted at 10°C resulted in a DT_{50} of 190 days (K24). When the 25°C data were normalised to 12°C, the predicted half-life is 280 days (using the equation (25) from TNG part II).

Under aerobic conditions, no significant extractable metabolites were produced in the soils treated with ^{14}C-benzoyl-hexaflumuron. However, in a supplemental experiment 2,6-difluorobenzoid acid was identified at levels up to 4% AR.

Soils treated with ^{14}C-aniline-hexaflumuron contained 12-20% of AR after 60-120 days as the major metabolite 3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenylamine, which decreased to 2-9% of AR after 365 days. A second, minor metabolite was present at ~4% of AR in soils treated with 14C-aniline-hexaflumuron. The major metabolite in the aerobic soil study conducted at 25 °C was the amine ((3,5-dichloro-4-(1,1,2,2)tetrafluoroethoxy)phenyl)amine), which reached a maximum at 30 DAT (M233 (sandy loam, 0.65% organic carbon), 12% AR), 60 DAT (Alconbury (clay loam, 1.87% organic carbon), 18%) and 120 DAT (M230 (silty loam, 1.57% organic carbon), 18% AR and Castle Rising (sandy loam, 8.62% organic carbon), 20 % AR). In soil M233, the amount of the amine at 30, 60, and 120 DAT was 12, 10, and 7% AR, respectively. In the Alconbury soil, the amine was present at 18 and 13% AR at 60 and 120 DAT, respectively. Modelling both formation and decline, the average half-life of the amine was calculated to be 43 days (geomean 38 days) while the average parent DT_{50} was 108 days (geomean 104 days) in these models, (note, there were negative confidence intervals (M233)). When normalised to 12 °C (using equation 25 of TNG part II), the DT_{50} for this metabolite was 107 days. (3,5-dichloro(1,1,2,2)tetrafluoro-ethoxy)phenyl)urea was identified at low levels, not greater than 5% through 120 DAT. The only degradate from the 14C-benzoyl-labeled hexaflumuron was 14CO2, plus very low levels (<5% AR) of 2,6-difluoro-benzoic acid.

Summarising three metabolites were identified - 1) as major metabolite (12-20% AR, day 60-120) 3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenylamine, calculation of half-life not possible, 2) as minor metabolite (≈4% AR) 3,5-dichloro-4-(1,1,2,2)-tetrafluoroethoxy) phenylurea, DT_{50} 34 days (25°C), 3) minor metabolite 2,6-difluorobenzoic acid, calculation of half-life not possible. The calculation of the half-life of the two metabolites was not possible due to a lack of data due to the low levels at which they were formed.

Abiotic degradation

Hexaflumuron is stable to hydrolysis under acidic conditions (pH = 5). Under neutral conditions (pH = 7), hexaflumuron slightly hydrolyses (6%), (DT_{50} = 270 days) and under basic conditions (pH = 9), hexaflumuron hydrolyses (DT_{50} = 22 days), with the resulting major components being the benzoic acid, benzamide, phenylurea, and phenylamine degradates.

Hexaflumuron photolyzes moderately in buffered (pH 5) water with the resulting major component being CO_2 and the difluorobenzamide and the hydroxyl-aniline degradates. The UV/VIS absorption spectra also show that there is a minimal absorption above 290 nm and no absorption above 316 nm. Aqueous photolysis will be an insignificant contributor to the degradation of hexaflumuron in the environment. The photolysis half-life in water for hexaflumuron was found to be approximately 6.3 days.

Hexaflumuron has low volatility (vapour pressure is 1.7 x 10^{-9} Pa at 18ºC) and emissions to the air compartment are expected to be very low from use. It has an estimated half-life of 6.1 hours therefore accumulation in the air is not to be expected.

Distribution

The hexaflumuron physico-chemical properties, such as the low vapour pressure, low water solubility, and high sorption, combined with the anticipated low rate use pattern of hexaflumuron in the bait systems, strongly suggest that hexaflumuron will not be present in environmental systems. The environmental distribution of hexaflumuron was examined using Level I and Level II fugacity models based on its physico-chemical properties and the results indicate that the majority of hexaflumuron released to the environment is predicted to be in the soil compartment (99%).

The desorption characteristics of hexaflumuron and metabolites were studied in four agricultural soils after aging for 30 days. The results show that hexaflumuron shows little tendency to desorb from soil into water (Kd = 147-1326), and therefore, little tendency to migrate through a soil/water column. The data also indicate that the metabolites, the amine and the phenylurea, have slight potential for movement (Kd = 35-392 and 32-142, respectively), and the benzoic acid (detected at 2-4% of AR in samples of 4 soils treated with 14C-benzoyl-labeled hexaflumuron) have a moderate potential for movement (Kd = 3-27).

In summary, the available adsorption/desorption data confirm that hexaflumuron is rapidly and strongly adsorbed to soil and is expected to be immobile in all soil types. Aged soil desorption resulted in Kd values above 147 mL/g and KdOC values above 3096 mL/g.

Using KOCWIN v2.00 (US EPA EPI Suite), a KOC value of 7272 L/kg was calculated. This value is probably conservatively low, since the adsorption KOC values for an analogue of hexaflumuron were >32,000 L/kg (noviflumuron, Log KOW 4.94).

Bioaccumulation

The log Kow (5.68 at 20 °C) and low water solubility (0.027 mg/L) predict a high bioconcentration factor in aquatic organisms. The BCF in fish was measured as 3783, 7667, and 5600 obtained for edible tissue, non-edible parts, and whole fish, respectively. On the basis of these findings hexaflumuron may be considered to bioconcentrate in aquatic species. From the octanol-water partition coefficient, the Log BCF in fish was estimated to be 13428 (Method by Veith et al, 1979), indicating also a potential for bioaccumulation. According to the TGD on risk assessment (Part II, Section 3.8.3), for substances with a log Kow ≥ 4.5, other uptake routes such as intake of contaminated food or sediment may become important.

The bioconcentration factor was calculated to be 6.8 x 10^{-6} mg/kg for predators. However, hexaflumuron is unlikely to enter any body of water, and will not be available to bioconcentrate in fish or other aquatic organisms.

According to the equation 82d from TGD, the BCFearthworm is 5744 L/kg wwt. This value for BCFearthworm could be overestimated, according to the section 3.8.3.7 of the Technical Guidance Document: "Jager (1998) has demonstrated that this approach performed very well in describing uptake in experiment with earthworms kept in water. For soil exposure, the scatter is larger and the experimental BCFs are generally somewhat lower than the predictions by the model."

2.2.2.2. Effects assessment

Aquatic compartment

Hexaflumuron is not acutely toxic to fish (bluegill sunfish 96h-LC_{50} > 141.86 µg/L and rainbow trout 96h-LC_{50} > 489.78 µg/L) and had no adverse effects on the biomass or growth rate of green algae (96h- ErC_{50} >1.91 mg a.s./L, in excess of the water solubility).

The acute toxicity studies show that Daphnia are significantly more sensitive to hexaflumuron than fish. This is likely due to the mode of action as hexaflumuron is a chitin synthase enzyme inhibitor and therefore not relevant to vertebrates. The vertebrate studies indicate that although hexaflumuron bioaccumulates in fish, it has very low toxicity to vertebrates and it is therefore logical that chronic exposure of fish would be less toxic than to Daphnia.

The toxicity of hexaflumuron to the bluegill sunfish was assessed under static conditions using concentrations of 100-500 µg/L. A solvent was used. Regarding the Bluegill study, the LC50 is greater than the highest nominal concentration tested (500 µg/L). The mean measured concentration of this treatment group was 468 µg/L at time 0 hours, and 43 µg/L at time 96 hours. Therefore, based on the geometric mean of these concentrations, the LC_{50} is >141.86 µg/L. It is important to note that a limit test was performed with Bluegill with a nominal concentration of 100 mg/L, which showed that even at this very high concentration in excess of the limit of water solubility, there was no mortality during the test.

Similarly, for the Rainbow Trout, the LC_{50} is greater than the highest nominal concentration tested (500 µg/L). The mean measured concentration in this treatment group at time 0 hours was 752 µg/L, and 319 µg/L at time 96 hours. Therefore, based on the geometric mean of these two mean measured concentrations, the LC_{50} is > 489.78 µg/L.

However hexaflumuron is highly toxic to daphnids in a 48h static acute toxicity test (EC_{50} = 0.11 µg/L) and 21-day semi-static exposure test (NOEC (adult survival) = 0.0029 µg/L; NOEC (reproduction) = 0.0029 µg/L; EC_{50} (reproduction) = 0.008 µg/L).

Hexaflumuron does not inhibit the aquatic microbial activity (activated sludge EC_{50} = 100mg/L).

$PNEC_{aquatic}$ was calculated from the long-term NOEC value for Daphnia, applying an assessment factor of 50, since two long-term NOEC values were available (daphnia and algae). The $PNEC_{aquatic}$ is 5.8 × 10^{-8} mg/L.

The $PNEC_{m\ croorganism}$ was calculated based on the result of the respiration inhibition test (NOEC > 100 mg/L), applying an assessment factor of 10. The $PNEC_{microorganism}$ is 10 mg/L.

The $PNEC_{sediment}$ was calculated using an AF of 1000, since only short-term toxicity tests were available. The $PNEC_{sediment}$ is 9.25 x 10^{-6} mg/kg and it was calculated using the partitioning method, as described in section 3.5.3 of the Technical Guidance Document on Risk Assessment, when no ecotoxicology data is available for sediment-dwelling organisms.

Terrestrial compartment

The studies on terrestrial organisms submitted by the applicant showed that hexaflumuron had no adverse effect on soil microflora activity and was non-toxic to earthworms, honeybees and non-target plants. In the bird studies, no effects were noted to Mallard ducks exposed to hexaflumuron in the diet for 5 days but the Northern Bobwhite was more sensitive than the duck with some mortality seen at high doses.

Short-term toxicity tests were conducted with hexaflumuron-exposed earthworms, soil microorganisms, and non-target plants. The $PNEC_{soil}$ was calculated based on the most environmentally relevant NOEC, earthworm. At The only dose evaluated in the acute earthworm toxicity study was 880 mg/kg dry soil. The assessment factor used was 1000, determined from Table 20 in section 3.6 of the Technical Guidance Document on Risk Assessment. The $PNEC_{soil\ (earthworm)}$ is 0.88 mg/kg.

Considering that the tested aquatic organisms included a crustacean, the $PNEC_{soil}$ was also calculated using the equilibrium partitioning method with a value of 2.92 x 10^{-5}mg/kg.

Non compartment specific effects relevant to the food chain (secondary poisoning)

Secondary poisoning to mammals was assessed using TOX_{oral} (equals the NOAEL x 8.3 BW/daily food intake). For hexaflumuron, the mammalian NOAEL of 25 mg/kg BW/day (subacute study- oral diet- of 13 weeks studies in mice and dogs, Ref. D4 and D5) results in a TOX_{oral} of 207.5 mg a.s./kg feed. Assuming an AF_{oral} of 90 (for a 90-day study) the $PNEC_{predator}$ is 2.3 mg/kg feed (mammals).

In relation to birds, the tested species were Mallard Duck and Bobwhite quail where no mortality was observed. According to Doc III A.7.5.5, TOX_{oral} equals the $NOEC_{bird}$ = 650 mg a.s./kg feed (Ref. J8), and the AF_{oral} = 30, yields a $PNEC_{predator}$ = 22 mg/kg feed (avian).

Due to the lack of exposure to bodies of water, secondary poisoning to mammals or birds from consumption of fish (aquatic food chain) is not a relevant exposure pathway.

2.2.2.3. PBT and POP assessment

PBT assessment

RMS considers that Hexaflumuron fulfils the criteria for all three inherent properties P, B and T.

Persistence

As to the persistence criteria, based on submitted studies (DocIIIA 7.2.1, 7.2.2.1, 7.2.2.3) Aerobic Biodegradation of soil, it indicates that hexaflumuron has an aerobic soil metabolism half-life of approximately 280 days (use of equation (25) of the TGD on Risk Assessment, part II, 2003, results in a geomean DT_{50} normalised to 12 °C of 280 days). According to the TGDs PBT criteria to P a substance is considered persistent if the degradation half-life in soil (or freshwater sediment) is higher than 120 days. Therefore, RMS considers that hexaflumuron fulfils the P criteria and the vP criteria as well.

Bioaccumulation

Regarding the Bioaccumulation, a substance fulfils the bioaccumulation criterion (B), when the bioconcentration factor (BCF) is higher than 2000. According to the study on bioconcentration in aquatic organisms (DocIIIA, 7.4.2), the BCF in fish was 3783, 7667 and 5600 for edible tissue, non-edible parts, and whole fish, respectively. RMS considers that the B and vB criteria is considerably fulfilled.

Toxicity

A substance fulfils the toxicity criterion (T) if chronic NOEC < 0.01 mg/L or CMR or endocrine disrupting effects. The daphnia 21d study (DocIIIA, 7.4.3.4) has a NOEC of 0.0029 µg/L therefore enabling the T criteria to be fulfilled.

POP assessment

The analysis of POPs criteria was not required when the dossier was evaluated and therefore not considered when Hexaflumuron was discussed at the environmental session of technical meeting (TMIV2013), since first RMS CAR was submitted before 1st of September 2013. Nevertheless, according to its atmospheric half-life (6.1 hours), hexaflumuron does not demonstrate the potential for long-range transport. In this view, hexaflumuron does not meet the criteria for being a persistent organic pollutant.

2.2.2.4. Exposure assessment

The environmental exposure has been assessed for the use of hexaflumuron in the RECRUTE™ Pro bait system (product type 18).

The environmental exposure to RECRUTE™ Pro baits containing hexaflumuron is primarily determined by the use pattern and the properties of the active ingredient. Since RECRUTE™ Pro baits are used only when and where termite activity is detected, as determined by untreated wood monitoring stations, the amount of product in the environment is extremely low, and particularly since each bait tube contains only 0.5% hexaflumuron. The majority of the RECRUTE™ bait tubes are used indoors, in enclosed plastic containers, further limiting exposure to the environment while protecting the residents.

The applicant provided the estimation of local emissions and the predicted environmental concentrations of hexaflumuron for the use of the termite control product, RECRUTE™ Pro, in surface water, groundwater and sediment, air and soil.

The active substance will enter the environment less by emissions from the baits but by the termites itself. The procedure of termite control is that the termites feed the active substance from the bait and pass it via trophallaxis to the other members of the colony. Additionally, there is no difference between indoor or outdoor application, since the termites do not live indoors, the colony is outdoors either around or underneath a structure.

The method for determining the local emissions and PEC was adapted from EUBEES (June 2000). Since the RECRUTE Pro bait system can be used indoors and outdoors, the product types "Baits used outdoors" and "Baits used in closed spaces and animal housings" are the only types relevant for products containing hexaflumuron. According to EUBEES document, the relevant emission routes for baits used outdoors are fresh surface water, soil, and solid waste and for baits used indoors, the relevant emission routes are air indoors and outdoors, solid waste, and waste water.

Nevertheless, there is no indoor exposure because the vapour pressure is extremely low and the termite colony is housed outdoors. The termites live in the soil (around or underneath the structure) and only come indoors to feed. The active substance is housed so as to prevent residents from contacting it.

The outdoor baits are placed in covered buckets, and the product remains in the bucket for consumption by termites; essentially no hexaflumuron in released to the environment.

However assuming 100% of hexaflumuron distribution, the local emissions were calculated (E_{local} = (# bait stations * Fai) where an average of 8 outdoor bait stations are used per structure); however the typical use is 2 bait stations at one time, each bait station contains 0.36 g hexaflumuron (0.5%). Therefore, the total hexaflumuron emitted (local) is 0.72g.

The local surface water emission was also estimated in case of leaching of hexaflumuron from outdoor bait stations. The fraction that may run-off was determined in the study which modelled the flooding of a bait station (DocIIIB, 7.4/01) in which less than 0.000053% of the hexaflumuron was detected in the water that leached from flooded cellulose bait over a small column of soil (Clocalsurfacewater = 5.088×10^{-10} g/m^3 (5.088×10^{-10} mg/L)).

The local soil concentration was calculated by using a fraction Fsoil=0.96 (in the adsorption/desorption study, more than 95% of hexaflumuron adsorbed to the soil) and Clocalsoil = 1.63×10^{-6} g/kg (0.00163 mg/kg). This result does not account for degradation of the hexaflumuron in the soil, and assumes that all of the bait is consumed by the termites/none is recovered for incineration.

Clocalsoil was calculated by considering the amount of hexaflumuron, which is required to eliminate a termite colony and the foraging range of the colony, an average of 0.5-1g of hexaflumuron. Considering the extreme foraging area of 2360m^2 and 1m^2, a soil incorporation of 1m (depth of termites within the soil), a soil density of 1.33g/cm^3, and 1g of active substance for a large colony and 0.1g a.s. for a small colony, the concentration of hexaflumuron in the soil ranges from 0.00032-0.075mg/kg (ppm). Therefore, the Clocalsoil ranges from 0.32-75 µg/kg, however, these results do not account for degradation of hexaflumuron in the soil or termites.

The emissions from placement of the baits indoors are considered negligible because 1) the vapour pressure of hexaflumuron is extremely low, 2) partially consumed baits are collected by the professional operators for eventual incineration. No hexaflumuron enters the wastewater or solid waste systems. Furthermore, model calculations have demonstrated that the air compartment will not be affected by hexaflumuron (DocIIIA, 7.3.1/01). Specifically the model shows no global warming potential, no ozone depletion in the stratosphere, no ozone formation in the troposphere, and no acidification.

The applicant also performed a Fugacity modelling (Mackay) to determine equilibrium concentrations in each of the environmental compartments. Fugacity modelling takes into account the fraction of hexaflumuron in the product that can be released to the environment, physical-chemical and environmental parameters such as vapour pressure and adsorption coefficients and therefore is effective at predicting the concentration in each compartment. Since the models used France as a representative geographic area, the results may be considered as PEC regional emission values (DocIIIB, 7.5/01).

The majority of hexaflumuron released to the environment was predicted to be in the soil compartment (99%). The sediment and suspended sediment are predicted to contain 0.99% and 0.0075%, respectively, of the mass of hexaflumuron released to the environment. Surface water, fish, and air are predicted to contain lower amounts of hexaflumuron, at 3.19×10^{-4}%, 6.13×10^{-4}%, and 1.05×10^{-9}%, respectively, of the mass of hexaflumuron released to the environment. The predicted equilibrium environmental concentrations of hexaflumuron in soil, sediment, and water, based on currently available degradation and emission rates, are 1.01×10^{-4} ng/g, 2.01×10^{-4} ng/g and 2.55×10^{-5} ng/L, respectively. Concerning the production of hexaflumuron (produced in the European Union – under contract for Dow AgroSciences by AlzChem Trostberg GmbH) the by-products HCl and CO will be passed through a scrubber and incinerated. Formulation of hexaflumuron into the termite bait is done outside Europe by Dow AgroSciences.

For the use of the termite control product, RECRUTE™ Pro, the applicant estimated the predicted environmental concentrations of hexaflumuron in water and sediment as 5.343×10^{-10} and 8.52×10^{-8} mg/L, respectively. The predicted environmental concentration of hexaflumuron in air was estimated as 3.1×10^{-12} ng/m3 and predicted environmental concentrations of hexaflumuron in soil as 1.63×10^{-3} mg/kg. Since hexaflumuron is applied as a bait formulation and seems to be immobile in soil, exposure would be limited to a small area in the close vicinity of the treated buildings. It could therefore be expected that the impact on soil organisms would not be extensive at the recommended use of RECRUTE™ Pro.

2.2.2.5. Risk characterisation

Aquatic compartment

Based on the available data, aquatic invertebrates are the most sensitive group.

Hexaflumuron will only be used in the SentriTech Termite Colony elimination System. The physical-chemical properties of hexaflumuron, such as the low water solubility and strong adsorption to soil, will prevent movement of hexaflumuron out of the bait stations. In addition, hexaflumuron that remains associated with the cellulose matrix (adsorbed) will be physically restrained from movement in the soil.

The PNECs values and PEC/PNEC ratios for local and regional water and for sediment and the results are well below the trigger value of 1, demonstrating no concern for aquatic organisms.

Table 01 - PEC/PNEC ratios for the aquatic and sediment compartments

PEC	PNEC	PEC/PNEC
$PEClocal_{water} = 5.343 \times 10^{-10}$ mg/L	$PNEC_{aquatic} = 5.8 \times 10^{-8}$ mg/L	$local_{water} = 9.21 \times 10^{-3}$
$PECregional_{water} = 2.55 \times 10^{-11}$ mg/L	$PNEC_{aquatic} = 5.8 \times 10^{-8}$ mg/L	$regional_{water} = 4.40 \times 10^{-4}$
$PEClocal_{sediment} = 8.52 \times 10^{-8}$ mg/L	$PNEC_{sediment} = 9.25 \times 10^{-6}$ mg/kg	$sediment = 9.21 \times 10^{-3}$
$PEClocal_{water} = 5.343 \times 10^{-10}$ mg/L	$PNEC_{STPmicroorganism} = 10$ mg/L	$STP_{microorganisms} = 5.3 \times 10^{-11}$

In summary, from the recommended use of the present formulation there is no release to water anticipated and consequently no risk to the aquatic compartment.

Atmosphere

Hexaflumuron is considered of low volatility (vapour pressure 5.87×10^{-9} Pa at 25 ºC) and does not absorb above 320 nm therefore, it is unlikely to be a potential greenhouse gas. The atmospheric half-life of hexaflumuron was calculated to be 6.1 hours, which would not allow time to transport to the stratospheric layer. Therefore, the risk to this compartment is of no-concern.

Terrestrial Compartment

Hexaflumuron is effective at eliminating a termite colony because the colony's worker caste is constantly searching for new food sources. Once worker termites locate the untreated wood monitoring devices, and it is subsequently replaced with the active substance, the "dosed" termites will take the hexaflumuron back to the colony. The hexaflumuron is efficiently passed through trophallaxis from one termite to another in the colony. The termites that have received a dose of hexaflumuron are prevented from molting. In any one treated colony, enough of the worker caste dies such that the colony can no longer survive due to poor health. The result is the death of the remaining colony even though the remainder has not received any dose of hexaflumuron. Furthermore, since hexaflumuron prevents moulting, termites that have received a dose of hexaflumuron cannot develop to the swarmer/alate stage, and therefore cannot leave the nest to swarm. The termites would die throughout the foraging area of the colony.

Short-term toxicity tests were conducted with hexaflumuron-exposed earthworms, soil microorganisms, and non-target plants. At the highest concentration tested in each of these studies, there were no adverse effects. The highest concentration evaluated for the soil microbial activity study was 2 mg/kg dry soil, or approximately 1200 times the PEC (PEClocalsoil = 1.63×10^{-3} mg/kg). The highest concentration for the non-target plant study was 100 g/ha, equivalent to 0.13 mg a.s./kg soil or approximately 80 times the PEC. The only dose evaluated in the acute earthworm toxicity study was 880 mg/kg dry soil.

The PNEC for soil was calculated to 0.88 mg/kg (most environmentally relevant NOEC, earthworm) applying an AF 1000 according to Table 20, section 3.6 of the Technical Guidance Document on Risk Assessment.

Considering that the tested aquatic organisms included a crustacean, the PNECsoil based on the equilibrium partitioning method is 2.92×10^{-5} mg/kg, assuming a Ksoil-water of 856.8 m^3/m^3.

Table 02 - PEC/PNEC ratios for the terrestrial compartment

PEC	PNEC	PEC/PNEC
$PEClocal_{soil}$ = 1.63×10^{-3} mg/kg	$PNEC_{soil}$ = 0.88 mg/kg (earthworms)	$local_{soil}$ = 1.85×10^{-3} (earthworms)
$PECregional_{soil}$ = 1.01×10^{-7} mg/kg	$PNEC_{soil}$ = 0.88 mg/kg (earthworms)	$regional_{soil}$ = 1.15×10^{-7} (earthworms)
$PEClocal_{soil}$ = 1.63×10^{-3} mg/kg	$PNEC_{soil}$ = 2.92×10^{-5} mg/kg (Equillibrium partitioning method)	$local_{soil}$ = 55.82 (Equillibrium partitioning method)

The most correct form is to use the lowest PNECsoil in the risk assessment for the soil compartment. In this case it is the PNECsoil based on equilibrium partitioning, which indicates a trigger value of PEC/PNEC >1, and a critical concern to terrestrial organisms.

Nevertheless, the use of PNECsoil based on the equilibrium partitioning method greatly overestimates the risk to soil-dwelling organisms. Soil-dwelling, moulting insects will only be sensitive while in the larval stage, and will not be exposed to hexaflumuron because the larvae will not burrow into the soil in order to feed on the in-ground stations (and will be too large to enter the slots of the bait holder and therefore unable to reach the bait), do not consume cellulose as a food source, nor will the larvae feed on dead termites.

Due to the use pattern of hexaflumuron in the bait stations, outdoor hexaflumuron-containing baits will only be used when and where termite activity has been detected. Therefore, terrestrial compartment organisms are unlikely to be exposed to hexaflumuron.

The applicant also performed several tests and showed that hexaflumuron had no adverse effect on soil microflora activity and is non-toxic to earthworms and honeybees.

In summary, there is a risk for the terrestrial compartment only considering the transport of hexaflumuron by the termites itself. Therefore, the most likely exposure scenario is soil residues from dead worker termites carrying hexaflumuron residues in the foraging area.

As to the risk characterization for groundwater, unlike a field application, installation of the SENTRITCH system is not uniform, and therefore the pore water concentration is not relevant. Data have demonstrated that hexaflumuron will bind rapidly and irreversibly to the first centimetre of soil around a bait station, indicating negligible concentration in the pore water surrounding the treated structure. The flooding of an in-ground bait station was simulated in an experimental study (Doc III B 7.4/01; K28). Columns with approximately 20 g light clay soil from France (Charentilly) were wetted, and then the hexaflumuron cellulose bait matrix added on top of the soil. The bait-soil combination was flooded and the water collected as above. The hexaflumuron concentration averaged 0.15 µg/L (non-detectable to 0.42 µg/L), or 0.00019% of the hexaflumuron present in the bait matrix. Soil acts both as a physical barrier to movement and as a sorption matrix as hexaflumuron strongly binds to soil (Reference: 98/8 CAR Doc. IIA, section 4.1.2 Adsorption/desorption and mobility in soil). The risk for ground water is not foreseen.

RMS considers that the assessment of PEC in groundwater as well as the risk assessment for groundwater is not necessary as the release of Hexaflumuron from b.p. RECRUTE Pro bait system to groundwater is negligible. In contrast, this might become relevant for further b.p. containing Hexaflumuron and should be assessed during national product authorisation. The applicant also agrees with this and confirm that there is no envisaged further use than termite control for hexaflumuron.

Non compartment specific effects relevant to the food chain (secondary poisoning)

Secondary poisoning concerns toxic effects in organisms at high trophic levels based on ingestion of organisms from lower trophic levels. Measured or predicted concentrations of residues in top predators are compared to no effect concentrations for the predators. The key components of the assessment of secondary poisoning are the assessment of potential bioaccumulation and potential toxicity of the substance following exposure to residues of the active substance.

Termite workers are well protected from vertebrate predation inside their mud tubes. Birds like woodpeckers may occasionally try to eat a few but they much prefer the large and slow larvae of bark beetle (Cerambycidae) to tiny and fast termite workers that escape rapidly when they are discovered[4]. Alate termites (adults) are a more vulnerable target to vertebrate predators, such as reptiles, birds and frogs[5] during the swarming phase, but workers that have ingested hexaflumuron will have died before adults stage as the active ingredients blocks molting and several molting are required to reach the adult stage.

Therefore, the most likely exposure scenario is soil residues from dead worker termites carrying hexaflumuron residues in the foraging area. Assuming uniform distribution of these residues, the risk assessment for non compartment specific effects relevant to the food chain (secondary poisoning) has been conducted with the conclusion that hexaflumuron is not expected to enter the food chain (PEC/PNEC ratio of hexaflumuron for terrestrial predators = 1.49×10^{-6} indicating there is negligible risk for secondary poisoning).

Since there is no direct or long-term exposure to soil, and the PNECpredator values for both mammals (2.3 mg/kg feed) and birds (22 mg/kg feed) are much greater than the PECpredator values, there is a huge safety factor of at least 1500000 regarding secondary terrestrial poisoning.

[4] Termites biologie, lutte règlementation from C Bordereau, JL Clément, M Jequel, F Viau
[5] Isoptera (termites) J.A.L. Watson and F.J. Gay

Table 03 - PEC/PNEC ratios for secondary poisoning

PEC	PNEC	PEC/PNEC
PECpredator = 3.42×10^{-6} mg/kgwet fish	PNECpredator = 2.3 mg/kg feed (mammals)	Oral = 1.49×10^{-6}

Due to the use pattern of hexaflumuron in the termite bait stations, outdoor hexaflumuron-containing baits will only be used when and where termite activity has been detected. Therefore, prey such as earthworms are unlikely to be exposed.

Although hexaflumuron appears to accumulate rapidly in lower trophic levels, it appears to depurate rapidly in fish. There are indications from available data that biomagnification does not occur to a great extent. Therefore, hexaflumuron is not expected to enter the food chain.

2.2.3. Assessment of endocrine disruptor properties

There is no indication from the mammalian toxicology studies that Hexaflumuron is an endocrine disruptor. Similarly, the mode of action is as a chitin synthase enzyme inhibitor and the additional literature information indicates that for benzyl-phenyl ureas chitin inhibition is non-endocrine for insects. Therefore, the applicant assumed that hexaflumuron does not possess endocrine disrupting properties.

The RMS suggests that the potential for endocrine disruption of hexaflumuron is reconsidered when EU harmonized guidance is established based on the work and final conclusions of the EC work on defining criteria to identify endocrine disruption substances.

2.3. Overall conclusions

a) Presentation of the active substance and representative biocidal product including classification[6] of the active substance

Hexaflumuron is a white odourless powder at room temperature. It is denser than water and undergoes no thermal decomposition below its melting temperature, which is in the region of 200°C. It decomposes below its boiling point. It was shown not to be technically feasible to accurately determine the dissociation constant due to the fact that the molecule does not contain reversible ionisable functional groups. Its vapour pressure is very low and hence its Henry's Law Constant indicates that volatilisation is not expected to significantly contribute to the dissipation of Hexaflumuron in the environment. Hexaflumuron is soluble in polar and non polar organic solvents. Hexaflumuron is not considered to possess explosive or oxidizing properties.

RECRUTE Pro is a ready for use product for professional application for the elimination of subterranean termite species including, though not exclusively: *Reticulitermes species, Coptotermes species,* and *Heterotemes species.*

RECRUTE Pro is a cellulose based bait (briquette) containing 0.5% of the active ingredient hexaflumuron. The bait is used both above ground and in ground stations.

[6] When the classification is presented, indicate the status (harmonised under CLP, under evaluation in the RAC etc).

Proposed classification for active substance based on Directive 67/548/EEC:

Classification:	N; R50/53
Hazard symbol:	N 
Class of danger:	N - Dangerous for the environment
R-phrases:	R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
Specific Concentration Limits	N; R50-53: C ≥ 0.025% N; R51-53: 0.0025% ≤ C < 0.025% R52-53: 0.00025% ≤ C < 0.0025%

Proposed classification for active substance based on CLP Regulation, under RAC consideration:

Classification		
Hazard Class and Category	Acute Aquatic Category 1 Chronic Aquatic Category 1	
H-Statements	H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects	
Labelling		
Signal Word	Warning	
Pictogram	GHS09	
H-Statements	H410: Very toxic to aquatic life with long lasting effects	
M-factors	Acute M-factor = 1 000 Chronic M-factor = 10 000	

Hexaflumuron has no entry in Annex VI of CLP Regulation; therefore, a registry of intentions was submitted to ECHA by Portugal, with an expected date of submission of the CLH dossier until the 28th of November 2014.

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

Hexaflumuron is used in products for insect control (Main Group 03, Product type 18, insecticides). The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against Reticulitermes species, Coptotermes species, and Heterotemes species in bait stations.

c) Risk characterisation for human health

Hexaflumuron has been evaluated in a series of toxicity studies of varying duration aimed at characterizing its hazard potential. Hexaflumuron was not acutely toxic as tested using oral dermal and inhalation routes of exposure and was not an eye irritant or dermal sensitizer. It was associated with very slight skin irritation, which was fully resolved by 7 days post-treatment. Hexaflumuron has been evaluated in repeated dose studies of varying duration using both rodent and non-rodent species. Following dietary (oral) exposure, the hemaetopoeitic system appears to be a target organ. NOAELs used in the risk assessment are listed below.

Test	NOAEL (mg/kg bw/day)	Endpoint
Short-term, based on the 28 day dietary dog study	8.3 (LOAEL of 25 mg/kg bw/day, NOAEL = 25 ÷ AF of 3)	Elevated methaemoglobin levels in both sexes and increased extramedullary haematopoiesis in spleen of males at next dose level and above.
Medium-term, based on the 13 week point of the 52 week dog dietary study	0.5	Dose-related increase in methemoglobin and hemosiderin deposits at next dose level with associated Heinz body formation at higher dose levels.
Long-term, based on the 52 week dog dietary study	0.5	Dose-related increase in methemoglobin and hemosiderin deposits at next dose level with associated Heinz body formation at higher dose levels.

Hexaflumuron was negative in all in vitro and in vivo mutagenicity and genotoxicity tests. Hexaflumuron was negative for tumorigenicity in both the rat and mouse. Hexaflumuron was not a developmental toxicant in either rats or rabbits and reproductive toxicity in rats was not a critical endpoint. Although hexaflumuron is not an organophosphate compound, it was evaluated for acute delayed neurotoxicity in the hen at a top dose of 5000 mg/kg. There were no indications of neurotoxicity, either clinically or following histopathological analysis.

Summary table: scenarios			
Scenario number	**Scenario**	**Primary or secondary exposure Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
1.	Installation	Primary exposure: Operator installs bait station. (i.e. mixing & loading of bait)	Professionals
2.	Inspection	Primary exposure: Operator inspects bait station	Professionals
3.	De-installation	Primary exposure: Operator removes bait from bait station	Professionals
4.	Mouthing of poison bait	Secondary exposure: Oral exposure to infant by mouthing of poison bait.	Bystanders (infants)
5.	Accidental ingestion	Secondary exposure: Oral exposure to infant by ingestion of unsecured bait.	Bystanders (infants)
6.	Accidental dermal contact	Secondary exposure: Short-term dermal exposure with bait	Bystanders (infants, children & adults)

Conclusion of risk characterisation for professional user

Scenario	**Relevant reference value**	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
1. Installation	AEL $_{short-term}$: 0.08 mg/kg bw/day	4.4×10^{-4}	0.6	Yes
	AEL $_{medium-term}$: 0.005mg/kg bw/day		8.8	Yes
	AEL $_{long-term}$: 0.005mg/kg bw/day		8.8	Yes
2. Inspection	AEL $_{short-term}$: 0.08 mg/kg bw/day	9.1×10^{-4}	1.1	Yes
	AEL $_{medium-term}$: 0.005mg/kg bw/day		18.4	Yes
	AEL $_{long-term}$: 0.005mg/kg bw/day		18.4	Yes
3. De-installation	AEL $_{short-term}$: 0.08 mg/kg bw/day	7.3×10^{-4}	0.9	Yes
	AEL $_{medium-term}$: 0.005mg/kg bw/day		14.7	Yes
	AEL $_{long-term}$: 0.005mg/kg bw/day		14.7	Yes

Conclusion of risk characterisation for non-professional user

Scenario	**Relevant reference value**[2]	**Estimated uptake** mg/kg bw/d	**Estimated uptake/reference value** (%)	**Acceptable** (yes/no)
Not Applicable				

Conclusion of risk characterisation for indirect exposure

Scenario	Relevant reference value[2]	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
4. Infant mouthing of poison bait	AEL $_{short-term}$: 0.08 mg/kg bw/day	0.002	2	Yes
5. Infant ingestion of unsecured bait	AEL $_{short-term}$: 0.08 mg/kg bw/day	0.83	1004	No

A reverse reference scenario was used as a Tier 1 Assessment for short-term dermal exposure to infant, child or adult that come into contact with the bait (see doc IIB for calculations). However, since the above ground station containing the product consists of a rigid plastic housing containing the bait matrix package and this tamper resistant closed bait station is fixed by screws and glued to the wall, such an exposure is unlikely to occur and the risk is considered mitigated.

The scenario used to assess infant acute exposure by mouthing of poisoning bait was similar to that used in rodenticides (PT14) bait box scenario listed in the TNsG, part 3, Appendix 7.2.1. Similarly to the dermal exposure, mouthing and accidental ingestion is unlikely to occur due to the design of the bait station and therefore risks are considered mitigated. Nonetheless, it is recommended to label the product with "Keep out of reach of children".

Conclusion on aggregated exposure
Not applicable.

Overall conclusion on human health risk characterization
The risk characterisation is considered to be sufficiently comprehensive and reliable for the purpose of annex I inclusion of hexaflumuron.

d) Risk characterisation for environment

Biodegradation

Hexaflumuron cannot be considered to be readily biodegradable and should be considered as persistent, having an aerobic soil metabolism half-life of approximately 280 days. The core aerobic soil studies were conducted at 25°C and were reanalyzed per latest FOCUS Kinetics guidance and recalculated using 0-120 day data only rather than 0-365 days according to OECD 307 study guidance (range 94 – 129 days (arithmean = 100 days, geomean = 99 days)). One test conducted at 10°C resulted in a DT_{50} of 190 days (K24). When the 25°C data were normalised to 12°C, the predicted half-life is 280 days (using the equation (25) from TNG part II).

Under aerobic conditions, no significant extractable metabolites were produced in the soils treated with ^{14}C-benzoyl-hexaflumuron. However, in a supplemental experiment 2,6-difluorobenzoid acid was identified at levels up to 4% AR.

Soils treated with ^{14}C-aniline-hexaflumuron contained 12-20% of AR after 60-120 days as the major metabolite 3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenylamine, which decreased to 2-9% of AR after 365 days. A second, minor metabolite was present at ~4% of AR in soils treated with 14C-aniline-hexaflumuron. The major metabolite in the aerobic soil study conducted at 25 °C was the amine ((3,5-dichloro-4-(1,1,2,2)tetrafluoroethoxy)phenyl)amine), which reached a maximum at 30 DAT (M233 (sandy loam, 0.65% organic carbon), 12% AR), 60 DAT (Alconbury (clay loam, 1.87% organic carbon), 18%) and 120 DAT (M230 (silty loam, 1.57% organic carbon), 18% AR and Castle Rising (sandy loam, 8.62% organic carbon), 20 % AR). In soil M233, the amount of the amine at 30, 60, and 120 DAT was 12, 10, and 7% AR, respectively. In the Alconbury soil, the amine was present at 18 and 13% AR at 60 and 120 DAT, respectively. Modeling both formation and decline, the average half-life of the amine was calculated to be 43 days (geomean 38 days) while the average parent DT_{50} was 108 days (geomean 104 days) in these models, (note, there were negative confidence intervals (M233)). When normalised to 12 °C (using equation 25 of TNG part II), the DT_{50} for this metabolite was 107 days. (3,5-dichloro(1,1,2,2)tetrafluoro-ethoxy)phenyl)urea was identified at low levels, not greater than 5% through 120 DAT. The only degradate from the 14C-benzoyl-labeled hexaflumuron was 14CO2, plus very low levels (<5% AR) of 2,6-difluoro-benzoic acid.

Summarising three metabolites were identified - 1) as major metabolite (12-20% AR, day 60-120) 3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenylamine, calculation of half-life not possible, 2) as minor metabolite (≈4% AR) 3,5-dichloro-4-(1,1,2,2)-tetrafluoroethoxy) phenylurea, DT_{50} 34 days (25°C), 3) minor metabolite 2,6-difluorobenzoic acid, calculation of half-life not possible. The calculation of the half-life of the two metabolites was not possible due to a lack of data due to the low levels at which they were formed.

Bioaccumulation

The log Kow (5.68 at 20 °C) and low water solubility (0.027 mg/L) predict a high bioconcentration factor in aquatic organisms. The BCF in fish was measured as 3783, 7667, and 5600 obtained for edible tissue, non-edible parts, and whole fish, respectively. On the basis of these findings hexaflumuron may be considered to bioconcentrate in aquatic species. From the octanol-water partition coefficient, the Log BCF in fish was estimated to be 13428 (Method by Veith et al, 1979), indicating also a potential for bioaccumulation. According to the TGD on risk assessment (Part II, Section 3.8.3), for substances with a log Kow ≥ 4.5, other uptake routes such as intake of contaminated food or sediment may become important.

The bioconcentration factor was calculated to be 6.8×10^{-6} mg/kg for predators. However, hexaflumuron is unlikely to enter any body of water, and will not be available to bioconcentrate in fish or other aquatic organisms.

According to the equation 82d from TGD, the BCFearthworm is 5744 L/kg wwt. This value for BCFearthworm could be overestimated, according to the section 3.8.3.7 of the Technical Guidance Document: "Jager (1998) has demonstrated that this approach performed very well in describing uptake in experiment with earthworms kept in water. For soil exposure, the scatter is larger and the experimental BCFs are generally somewhat lower than the predictions by the model."

Aquatic compartment

Hexaflumuron is not acutely toxic to fish (bluegill sunfish 96h-LC_{50} > 141.86 µg/L and rainbow trout 96h-LC_{50} > 489.78 µg/L) and had no adverse effects on the biomass or growth rate of green algae (96h- ErC_{50} >1.91 mg a.s./L, in excess of the water solubility).

The acute toxicity studies show that Daphnia are significantly more sensitive to hexaflumuron than fish. This is likely due to the mode of action as hexaflumuron is a chitin synthase enzyme inhibitor and therefore not relevant to vertebrates. The vertebrate studies indicate that although hexaflumuron bioaccumulates in fish, it has very low toxicity to vertebrates and it is therefore logical that chronic exposure of fish would be less toxic than to Daphnia.

The toxicity of hexaflumuron to the bluegill sunfish was assessed under static conditions using concentrations of 100-500 μg/L. A solvent was used. Regarding the Bluegill study, the LC_{50} is greater than the highest nominal concentration tested (500 μg/L). The mean measured concentration of this treatment group was 468 μg/L at time 0 hours, and 43 μg/L at time 96 hours. Therefore, based on the geometric mean of these concentrations, the LC_{50} is >141.86 μg/L. It is important to note that a limit test was performed with Bluegill with a nominal concentration of 100 mg/L, which showed that even at this very high concentration in excess of the limit of water solubility, there was no mortality during the test.

Similarly, for the Rainbow Trout, the LC_{50} is greater than the highest nominal concentration tested (500 μg/L). The mean measured concentration in this treatment group at time 0 hours was 752 μg/L, and 319 μg/L at time 96 hours. Therefore, based on the geometric mean of these two mean measured concentrations, the LC_{50} is > 489.78 μg/L.

However hexaflumuron is highly toxic to daphnids in a 48h static acute toxicity test (EC_{50} = 0.11 μg/L) and 21-day semi-static exposure test (NOEC (adult survival) = 0.0029 μg/L; NOEC (reproduction) = 0.0029 μg/L; EC_{50} (reproduction) = 0.008 μg/L).

Hexaflumuron does not inhibit the aquatic microbial activity (activated sludge EC_{50}=100mg/L).

$PNEC_{aquatic}$ was calculated from the long-term NOEC value for Daphnia, applying an assessment factor of 50, since two long-term NOEC values were available (daphnia and algae). The $PNEC_{aquatic}$ is 5.8 × 10^{-8} mg/L.

The $PNEC_{m\ croorganism}$ was calculated based on the result of the respiration inhibition test (NOEC > 100 mg/L), applying an assessment factor of 10. The $PNEC_{microorganism}$ is 10 mg/L.

The $PNEC_{sediment}$ was calculated using an AF of 1000, since only short-term toxicity tests were available. The $PNEC_{sediment}$ is 9.25 x 10^{-6} mg/kg and it was calculated using the partitioning method, as described in section 3.5.3 of the Technical Guidance Document on Risk Assessment, when no ecotoxicology data is available for sediment-dwelling organisms.

Terrestrial compartment

The studies on terrestrial organisms submitted by the applicant showed that hexaflumuron had no adverse effect on soil microflora activity and was non-toxic to earthworms, honeybees and non-target plants. In the bird studies, no effects were noted to Mallard ducks exposed to hexaflumuron in the diet for 5 days but the Northern Bobwhite was more sensitive than the duck with some mortality seen at high doses.

Short-term toxicity tests were conducted with hexaflumuron-exposed earthworms, soil microorganisms, and non-target plants. The $PNEC_{soil}$ was calculated based on the most environmentally relevant NOEC, earthworm. At The only dose evaluated in the acute earthworm toxicity study was 880 mg/kg dry soil. The assessment factor used was 1000, determined from Table 20 in section 3.6 of the Technical Guidance Document on Risk Assessment. The PNECsoil (earthworm) is 0.88 mg/kg.

Considering that the tested aquatic organisms included a crustacean, the $PNEC_{soil}$ was also calculated using the equilibrium partitioning method with a value of 2.92 x 10^{-5}mg/kg.

Non compartment specific effects relevant to the food chain (secondary poisoning)

Secondary poisoning to mammals was assessed using TOXoral (equals the NOAEL x 8.3 BW/daily food intake). For hexaflumuron, the mammalian NOAEL of 25 mg/kg BW/day (subacute study- oral diet- of 13 weeks studies in mice and dogs, Ref. D4 and D5) results in a TOXoral of 207.5 mg a.s./kg feed. Assuming an AForal of 90 (for a 90-day study) the PNECpredator is 2.3 mg/kg feed (mammals).

In relation to birds, the tested species were Mallard Duck and Bobwhite quail where no mortality was observed. According to Doc III A.7.5.5, TOXoral equals the NOECbird = 650 mg a.s./kg feed (Ref. J8), and the AForal = 30, yields a PNECpredator = 22 mg/kg feed (avian).

Due to the lack of exposure to bodies of water, secondary poisoning to mammals or birds from consumption of fish (aquatic food chain) is not a relevant exposure pathway.

Compartment	PNEC
$PNEC_{aquatic}$	5.8×10^{-8} mg/L
$PNEC_{microorganism}$	10 mg/L
$PNEC_{sediment}$	9.25×10^{-6} mg/kg
$PNEC_{soil\ (earthworm)}$	0.88 mg/kg
$PNEC_{soil\ (equilibrium\ partitioning\ method)}$	2.92×10^{-5}mg/kg
$PNEC_{predator\ (mammals)}$	2.3 mg/kg feed
$PNEC_{predator\ (avian)}$	22 mg/kg feed

	Summary table on calculated PEC/PNEC values					
	PEC/PNEC stp	PEC/PNEC sw	PEC/PNEC sed	PEC/PNEC soil (earthworm)	PEC/PNEC soil (eq. part. met.)	PEC/PNEC Pred
Scenario 1	5.3×10^{-11}	9.21×10^{-3}	9.21×10^{-3}	1.85×10^{-3}	55.82	1.49×10^{-6}

Conclusion on aggregated exposure

The environmental exposure has been assessed for the use of hexaflumuron in the RECRUTE™ Pro bait system (product type 18).

The environmental exposure to RECRUTE™ Pro baits containing hexaflumuron is primarily determined by the use pattern and the properties of the active ingredient. Since RECRUTE™ Pro baits are used only when and where termite activity is detected, as determined by untreated wood monitoring stations, the amount of product in the environment is extremely low, and particularly since each bait tube contains only 0.5% hexaflumuron. The majority of the RECRUTE™ bait tubes are used indoors, in enclosed plastic containers, further limiting exposure to the environment while protecting the residents.

The applicant provided the estimation of local emissions and the predicted environmental concentrations of hexaflumuron for the use of the termite control product, RECRUTE™ Pro, in surface water, groundwater and sediment, air and soil.

The active substance will enter the environment less by emissions from the baits but by the termites itself. The procedure of termite control is that the termites feed the active substance from the bait and pass it via trophallaxis to the other members of the colony. Additionally, there is no difference between indoor or outdoor application, since the termites do not live indoors, the colony is outdoors either around or underneath a structure.

The method for determining the local emissions and PEC was adapted from EUBEES (June 2000). Since the RECRUTE Pro bait system can be used indoors and outdoors, the product types "Baits used outdoors" and "Baits used in closed spaces and animal housings" are the only types relevant for products containing hexaflumuron. According to EUBEES document, the relevant emission routes for baits used outdoors are fresh surface water, soil, and solid waste and for baits used indoors, the relevant emission routes are air indoors and outdoors, solid waste, and waste water.

Nevertheless, there is no indoor exposure because the vapour pressure is extremely low and the termite colony is housed outdoors. The termites live in the soil (around or underneath the structure) and only come indoors to feed. The active substance is housed so as to prevent residents from contacting it.

The outdoor baits are placed in covered buckets, and the product remains in the bucket for consumption by termites; essentially no hexaflumuron in released to the environment.

However assuming 100% of hexaflumuron distribution, the local emissions were calculated (E_{local} = (# bait stations * Fai) where an average of 8 outdoor bait stations are used per structure); however the typical use is 2 bait stations at one time, each bait station contains 0.36 g hexaflumuron (0.5%). Therefore, the total hexaflumuron emitted (local) is 0.72g.

The local surface water emission was also estimated in case of leaching of hexaflumuron from outdoor bait stations. The fraction that may run-off was determined in the study which modelled the flooding of a bait station (DocIIB, 7.4/01) in which less than 0.000053% of the hexaflumuron was detected in the water that leached from flooded cellulose bait over a small column of soil (Clocalsurfacewater = 5.088 x 10^{-10} g/m^3 (5.088 x 10^{-10} mg/L)).

The local soil concentration was calculated by using a fraction Fsoil=0.96 (in the adsorption/desorption study, more than 95% of hexaflumuron adsorbed to the soil) and Clocalsoil = 1.63 x 10^{-6} g/kg (0.00163 mg/kg). This result does not account for degradation of the hexaflumuron in the soil, and assumes that all of the bait is consumed by the termites/none is recovered for incineration.

Clocalsoil was calculated by considering the amount of hexaflumuron, which is required to eliminate a termite colony and the foraging range of the colony, an average of 0.5-1g of hexaflumuron. Considering the extreme foraging area of 2360m^2 and 1m^2, a soil incorporation of 1m (depth of termites within the soil), a soil density of 1.33g/cm^3, and 1g of active substance for a large colony and 0.1g a.s. for a small colony, the concentration of hexaflumuron in the soil ranges from 0.00032-0.075mg/kg (ppm). Therefore, the Clocalsoil ranges from 0.32-75 µg/kg, however, these results do not account for degradation of hexaflumuron in the soil or termites.

The emissions from placement of the baits indoors are considered negligible because 1) the vapour pressure of hexaflumuron is extremely low, 2) partially consumed baits are collected by the professional operators for eventual incineration. No hexaflumuron enters the wastewater or solid waste systems. Furthermore, model calculations have demonstrated that the air compartment will not be affected by hexaflumuron (DocIIIA, 7.3.1/01). Specifically the model shows no global warming potential, no ozone depletion in the stratosphere, no ozone formation in the troposphere, and no acidification.

The applicant also performed a Fugacity modelling (Mackay) to determine equilibrium concentrations in each of the environmental compartments. Fugacity modelling takes into account the fraction of hexaflumuron in the product that can be released to the environment, physical-chemical and environmental parameters such as vapour pressure and adsorption coefficients and therefore is effective at predicting the concentration in each compartment. Since the models used France as a representative geographic area, the results may be considered as PEC regional emission values (DocIIB, 7.5/01).

The majority of hexaflumuron released to the environment was predicted to be in the soil compartment (99%). The sediment and suspended sediment are predicted to contain 0.99% and 0.0075%, respectively, of the mass of hexaflumuron released to the environment. Surface water, fish, and air are predicted to contain lower amounts of hexaflumuron, at 3.19 x 10^{-4}%, 6.13 x 10^{-4}%, and 1.05 x 10^{-9}%, respectively, of the mass of hexaflumuron released to the environment. The predicted equilibrium environmental concentrations of hexaflumuron in soil, sediment, and water, based on currently available degradation and emission rates, are 1.01 x 10^{-4} ng/g, 2.01 x 10^{-4} ng/g and 2.55 x 10^{-5} ng/L, respectively. Concerning the production of hexaflumuron (produced in the European Union – under contract for Dow AgroSciences S.A. by AlzChem Trostberg GmbH) the by-products HCl and CO will be passed through a scrubber and incinerated. Formulation of hexaflumuron into the termite bait is done outside Europe by Dow AgroSciences.

For the use of the termite control product, RECRUTE™ Pro, the applicant estimated the predicted environmental concentrations of hexaflumuron in water and sediment as 5.343 x 10^{-10} and 8.52 x 10^{-8} mg/L, respectively. The predicted environmental concentration of hexaflumuron in air was estimated as 3.1 x 10^{-12} ng/m3 and predicted environmental concentrations of hexaflumuron in soil as 1.63 x 10^{-3} mg/kg. Since hexaflumuron is applied as a bait formulation and seems to be immobile in soil, exposure would be limited to a small area in the close vicinity of the treated buildings. It could therefore be expected that the impact on soil organisms would not be extensive at the recommended use of RECRUTE™ Pro.

Overall conclusion on environment risk characterization

Hexaflumuron is highly toxic for aquatic organisms (aquatic invertebrates are the most sensitive group) but no direct release to the aquatic compartment is expected. Additionally, its physical-chemical properties, such as the low water solubility and strong adsorption to soil, will prevent movement of hexaflumuron out of the bait stations. Therefore, no risk is identified to the aquatic compartment.

No risk is identified to the air compartment as well, considering the low volatility, no absorption above 320 nm and the atmospheric half-life of hexaflumuron (6.1 hours).

Two PEC/PNEC values for the terrestrial compartment were obtained, based on earthworm test and equilibrium partitioning method. The last method demonstrates a potential risk of hexaflumuron to this compartment. Nevertheless, the use of PNECsoil based on the equilibrium partitioning method greatly overestimates the risk to soil-dwelling organisms. Several tests showed that hexaflumuron had no adverse effect on soil microflora activity and is non-toxic to earthworms and honeybees. In summary, there is a risk for the terrestrial compartment only considering the transport of hexaflumuron by the termites itself. Therefore, the most likely exposure scenario is soil residues from dead worker termites carrying hexaflumuron residues in the foraging area.

The risk for groundwater is not foreseen since hexaflumuron will bind rapidly and irreversibly to the soil around a bait station. RMS considers that the assessment of PEC in groundwater as well as the risk assessment for groundwater is not necessary as the release of Hexaflumuron from b.p. RECRUTE Pro bait system to groundwater is negligible.

Assuming uniform distribution of soil residues from dead worker termites carrying hexaflumuron residues in the foraging area, the risk assessment for non-compartment specific effects relevant to the food chain (secondary poisoning) has been conducted with the conclusion that hexaflumuron is not expected to enter the food chain. Due to the use pattern of hexaflumuron in the termite bait stations, outdoor hexaflumuron-containing baits will only be used when and where termite activity has been detected. Therefore, prey such as earthworms are unlikely to be exposed.

Although hexaflumuron appears to accumulate rapidly in lower trophic levels, it appears to depurate rapidly in fish. There are indications from available data that biomagnification does not occur to a great extent.

e) Substitution and exclusion criteria

Hexaflumuron is a PBT, a vB (based on the BCF > 5000) and a vP (DT_{50} > 180 in soil when normalised to 12 °C), thus fulfilling the exclusion criteria of Article 5(1)(e) of BPR. Despite of its properties, this active substance can be included in the "Union list of approved active substances" since it meets at least one of the conditions presented in Article 5(2) of BPR (see section f) overall conclusion evaluation, below). Considering this, Hexaflumuron has been identified as a Candidate for Comparative Assessment and for Substitution.

f) Overall conclusion evaluation including need for risk management measures

Due to the use pattern of hexaflumuron in the termite bait stations, outdoor hexaflumuron-containing baits stations will only be used when and where termite activity has been detected. Hexaflumuron is highly toxic for aquatic organisms and fulfils the PBT and the vPvB criteria, but no direct release to the aquatic compartment is expected, as well as for terrestrial or air compartments. The physical-chemical properties of hexaflumuron, such as the low water solubility and strong adsorption to soil, will prevent movement of hexaflumuron out of the bait stations. In addition, hexaflumuron that remains associated with the cellulose matrix (adsorbed) will be physically restrained from movement in the soil.

In summary, no risk for the aquatic and air compartments is identified for the use of hexaflumuron. The only potential risk identified will be for the terrestrial compartment, although this will only occur through the transport of hexaflumuron by the termites itself.

RMS considers that, although Hexaflumuron is a PBT, a vB (based on the BCF > 5000) and a vP (DT50 > 180 in soil when normalised to 12 °C), there are strong reasons to support the inclusion of hexaflumuron in the "Union list of approved active substances", with some restrictions.

In fact, according to article 5(2) of BPR, a PBT or vPvB substance could be included in the "Union list of approved active substances" if at least one of the following conditions is met:

a) *The risk to humans, animals or the environment from exposure to the active substance in a biocidal product, under realistic worst case conditions of use, is negligible, in particular where the product is used in closed systems or under other conditions which aim at excluding contact with humans and release into the environment*.

   Hexaflumuron is placed in the market in enclosed bait systems, minimising exposure to humans, animals or the environment. Using a bait station the active ingredient cannot get into environment as shown in the flooded bait study. The only possible spread would be through the termites themselves.

   For the control of termites, there are only two control measures available, baits and drench treatments, the latter using very high volumes of active substance and resulting in higher exposure. Therefore, the use of bait, with a minimal amount of a.s., is preferred, since there is no direct exposure to soil, there is no direct exposure to water, and there is no potential for atmospheric transport or deposition.

   The use and the waste disposal of a termite bait treatment recommendations of the manufacturer are such that the exposure is kept to negligible levels (ex: initial baiting with plain wood which gets replaced only when termites have found to start eating).

b) *The active substance is essential to control a serious danger.*

   Termites are widespread in Southern Europe. France, Italy and Spain being the most infested countries.

Termites are very difficult to control and damage not only private homes but also historic buildings and sites. These structures, if left untreated, would be unsafe for habitation.

Hexaflumuron has been proved to be a very effective active substance, and available active substances in Europe for use in termite control (colony elimination systems) are very limited in number and efficacy.

Available active ingredients in Europe for use in termite baits (colony elimination systems) are very limited (currently 2 active ingredients listed Annex I in PT18 for termite control (diflubenzuron and fipronil). Fipronil is used in drench treatments (physically drenching the surrounding of the structure / or injecting the insecticide into the house walls with quantities7 of the substance using a hose) and cannot be compared with a products used in a bait station. The other active on Annex I is diflubenzuron, used in a bait station like hexaflumuron. Only hexaflumuron is certified by the French FCBA Institute Technologique (www.ctbpplus.fre) to be effective both on species of continental European termite species (Reticulitermes spp.) and tropical species like Coptotermes spp. Not having hexaflumuron available would render impossible to control all damaging species of termites. As there are no alternative substances available, the use of hexaflumuron is essential, regarding that it should be considered as a Candidate for Substitution and Comparative Assessment.

c) *Not approving the inclusion of the active substance would have a disproportional negative impact on society.*

As previously stated termites are very difficult to control and can cause high damage to private homes and historic buildings. These structures, if left untreated, would also cause big financial constraints since termite infested structures have a low market value and cause significant impact on society, where historical buildings are concerned.

Recently historic structures were treated with hexaflumuron e.g. the cathedral of Santiago de Compostella (Spain), University of Sorbonne in Paris and historical center of Bourges (France), historical center of Bagnacavalli (Italy). Therefore, Hexaflumuron can contribute to the maintenance of European national heritage.

Taking into consideration the justifications above, the Portuguese CA proposes to include Hexaflumuron (CAS n.º 86479-06-3) in the "Union list of approved active substances", under BPR, for 5 years, as an active substance for use in product-type 18 (insecticide), subject to the following specific provisions:

- The active substance hexaflumuron as manufactured shall have a minimum purity of 984g/kg.
- The product should be designed in such a way that the exposure of hexaflumuron to humans and the environment will be negligible (confined tamper resistant bait station).
- It should only be handled by professionals.
- The active substance must not be used in treated articles.
- The nano-form of the active substance shall not be considered as covered by the approval.
- The active substance must not be subject to inclusion in Annex I of BPR.

[7] FCBA France listed as: Termidor SC, 9 % fipronil, masonry & soil injection, 0.1-0.2 % w/w, the amount of product diluted in water is 100 kg/m^3 for the treatment of walls and 51 kg/m^2 (5 cm deep) for soil treatment (also equal to 100 kg/m^3)

Without prejudice of this inclusion, RMS also considers that, due to the PBT properties, Hexaflumuron shall be listed as a Candidate for Substitution and Comparative Assessment will have to be conducted at Member State level.

2.4. List of endpoints

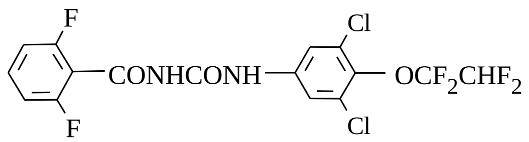
The most important endpoints, as identified during the evaluation process, are listed in Appendix I.

Appendix I: List of endpoints

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

Active substance (ISO Common Name)	Hexaflumuron
Product-type	Insecticide (PT18)

Identity

Chemical name (IUPAC)	1-[3,5-dichloro-4-(1,1,2,2-tetrafluoroethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea
Chemical name (CA)	Benzamide, N-[[[3,5-dichloro-4-(1,1,2,2-tetrafluoroetho-xy)phenyl]amino]carbonyl]-2,6-difluoro-
CAS No	86479-06-3
EC No	401-400-1 (EEC)
Other substance No.	XDE-473 (experimental code)
Minimum purity of the active substance as manufactured (g/kg or g/l)	984 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	The 5-batch analysis identified three impurities present in quantities of 1 g/kg or higher. Please see Confidential Annex.
Molecular formula	C16 H8 Cl2 F6 N2 O3
Molecular mass	461.1 g/mol
Structural formula	

Physical and chemical properties

Melting point (state purity)	202 – 205 °C (98.2%)
Boiling point (state purity)	The sample decomposes after melting, before it is able to boil.
Temperature of decomposition	Decomposes without boiling above the melting point.
Appearance (state purity)	White odourless powder at room temperature (98.2%)
Relative density (state purity)	1.680 g/cm3 at 20 °C (98.2%)
Surface tension	Very low water solubility, hence study not conducted
Vapour pressure (in Pa, state temperature)	1.7×10^{-9} Pa at 18 °C 5.9×10^{-9} Pa at 25 ºC
Henry's law constant (Pa m^3 mol^{-1})	2.9×10^{-5} $Pa.m^3mol^{-1}$
Solubility in water (g/l or mg/l, state temperature)	2.7×10^{-5} g/L at 18 °C. pH: 9.77
Solubility in organic solvents (in g/l or mg/l, state temperature)	<u>Solvents</u> — <u>solubility (mg/L)</u> Acetone — >100000 Acetonitrile — 14600 Dichloromethane — 12600 Ethyl acetate — >100000 Hexane — 7 Methanol — 11300 Propan-2-ol — 3000 1-Octanol — 2000 Toluene — 6400 Xylene — 5200
Stability in organic solvents used in biocidal products including relevant breakdown products	Not applicable. Active substance is not formulated in solvents in biocidal products
Partition coefficient (log P_{OW}) (state temperature)	5.462 at 24 °C
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH 5: stable
	pH 7: 270 days at 25 °C
	pH 9: 22 days at 25 °C
Dissociation constant	Cannot be determined. Molecule does not contain reversible ionisable functional groups.
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	<u>Methanol</u> <u>pH</u> <u>Abs Max</u> <u>Ext Coeff ($Lmol^{-1}$ cm^{-1})</u> Acidi 0.83 253.4 1.92×10^4 208.4 3.95×10^4 Basic 12.93 249.6 1.60×10^4 218.8 3.02×10^4 Methanolic 7.45 253.2 1.91×10^4 209.2 3.95×10^4
Photostability (DT_{50}) (aqueous, sunlight, state pH)	half-life ca. 6.3 days in summer sunlight (pH 5 buffer)

Quantum yield of direct phototransformation in water at > 290 nm	1.5 x 10^{-2} (buffered water)
Flammability	Not flammable, not autoflammable
Explosive properties	no explosive for thermal or mechanical (shock) sensitivity, but sensitivity to mechanical (friction)

Classification and proposed labelling based on Dir. 67/548/EEC (Annex IIA, point IX.)

with regard to physical/chemical data	None.
with regard to toxicological data	
with regard to fate and behaviour data with regard to ecotoxicological data	Dangerous for the environment R50/53 (Very toxic to aquatic organisms, may cause long-term effects in aquatic environment)

Classification and proposed labelling based on CLP Regulation (Annex IIA, point IX)

with regard to physical/chemical data	None.
with regard to toxicological data	
with regard to fate and behaviour data with regard to ecotoxicological data	Acute Aquatic 1; H400: Very toxic to aquatic life Chronic Aquatic 1; H410: Very toxic to aquatic life with long lasting effects. Acute M-factor = 1000 Chronic M-factor = 10 000

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	Method using reversed-phase, isocratic, liquid chromatographic separation with UV detection with a Spherisorb ODS2 column to separate hexaflumuron and related impurities. Octaphenone is used as an internal standard and the analytes are detected using a wavelength of 255 nm. The method was suitably validated.
Impurities in technical active substance (principle of method)	Method using a reversed-phase, isocratic, liquid chromatographic separation with UV detection and a Spherisorb ODS2 column. Octaphenone is used as an internal standard and the analytes are detected using a wavelength of 235 nm. The method was suitable validated.

Analytical methods for residues

Soil (principle of method and LOQ)	GRM 06.07 - Quantitative determination of Residues of Hexaflumuron in Sediment and Soil by Liquid Chromatography with Tandem Mass Spectrometry Detection- LOD 0.010 µg/g.
Air (principle of method and LOQ)	No method was submitted due to hexaflumuron low vapour pressure [1.7 x 10-9 Pa at 18ºC (purity: 99.3 %)] and Fugacity modelling results which confirmed that only 1.05 x 10-9% of the hexaflumuron present in the environment will be in the air compartment.
Water (principle of method and LOQ)	Method Validation of the determination of

	Residues of Hexaflumuron in Ground, Surface, Drinking and Flooded Bait Water Using Liquid Chromatography with Tandem Mass Spectrometry: Surface water - LOQ 0.001 µg/L Groundwater - LOQ 0.001 µg/L Drinking water – LOQ 0.001 µg/L Flooded bait water - LOQ 0.001 µg/L.
Body fluids and tissues (principle of method and LOQ)	No analytical methods for animal and human body fluids and tissues were submitted because hexaflumuron is not classified as Toxic to humans and due to use pattern of hexaflumuron enclosed in bait stations.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	The termite bait product will not be used in/on food or feedstuffs or near food or feedstuffs, nor in/on/near any food/feedstuffs packaging. Not required.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	The termite bait product will not be used in/on food or feedstuffs or near food or feedstuffs, nor in/on/near any food/feedstuffs packaging. Not required.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Three ADME studies (mouse, rat, dog) by single oral dose were submitted. Hexaflumuron is well-absorbed in the rat following oral administration at low (5 mg/kg bw) dose levels, but saturation occurs at higher (250 mg/kg bw) dose levels resulting in substantially less absorption. Single oral (gavage) exposure of 5 mg/kg bw in rats and mice result in absorptions higher than 80% and 90% respectively. Oral absorption estimation in the dog was not possible due to study limitations. Peak plasma levels in all three species are similar, occurring from 4-8 hours following exposure. Plasma AUC from a 250 mg/kg bw dose is 4-5 times that from a 5 mg/kg bw dose. Elimination from the blood follows first-order kinetics with half-lives in all 3 species ranging from 14-30 hours depending on the specific radiolabelled material used.
Rate and extent of dermal absorption for the active substance:	There is no direct measure of dermal penetration for hexaflumuron. A 12.5% dermal penetration based on the OECD and EFSA scientific opinion notes on dermal absorption (OECD Report ENV/JM/MONO(2011)36 & EFSA Journal 2011: 9(7): 2294). This value is calculated using the 3 week rat dermal study with LOAEL of >1000 mg/kg/day together with the 13 week rat oral study with LOAEL of 125 mg/kg/day
Rate and extent of inhalation absorption for the representative product(s)[8]:	There is no direct measure of inhalation absorption for hexaflumuron. Therefore, a 100% absorption following inhalation exposure was assumed for risk assessment.
Distribution:	Distribution of hexaflumuron is characterized as moderate with recoveries seen predominantly in liver>kidney>fat (rat data). Higher dose levels resulted in greater tissue presence. Hexaflumuron in the blood appears to be associated with the plasma, with no evidence of accumulation in the blood cells.
Potential for accumulation:	Given the saturation of absorption at higher dose levels, coupled with the extensive metabolism and excretion profile for hexaflumuron, bioaccumulation is not expected to occur.
Rate and extent of excretion:	Both urinary and fecal excretions are involved in the elimination of hexaflumuron. Following oral (gavage) low-dose administration urinary excretion ranges from 27-39% in the rat, to 15-63% in the mouse and from 1 - 5% in the dog depending on the specific radiolabelled material used. Similarly, fecal excretion following oral

[8] Please consider Q5 on *Derivation of dermal absorption values* of section 4.1.1 of the Manual of Technical Agreements (MOTA) version 5.

	(gavage) low-dose administration ranges from 47-58% in the rat, to 24-67% in the mouse to approximately 69% in the dog. In the dog dietary study, urinary excretion at the low dose ranged from 19- 51%. The radioactivity excreted via the feces ranged from 37- 64% for the low dose. No parent compound was present in the urine and only 8-14% of the parent compound was present in the feces.
Toxicologically significant metabolite(s)	None

Acute toxicity

Rat LD_{50} oral	LD50 > 5000 mg/kg bw
Rat LD_{50} dermal	LD50 > 2000 mg/kg bw
Rat LC_{50} inhalation	LC50 > 7 mg/L
Skin irritation	Not classified
Eye irritation	Not classified
Skin sensitization (test method used and result)	Negative in the modified Buehler test

Repeated dose toxicity

Species/ target / critical effect	Repeated exposure to hexaflumuron has been investigated by the oral route in subacute studies (rats, mice, and dogs), in subchronic studies (mice and rats) and in chronic studies (rats and dogs). Increased methemoglobin (MetHb) was the major finding in all studies and considered as the critical adverse effect for the risk assessment and NOAEL setting. The lowest relevant NOAEL (used to set the long-term AEL) was 0.5 mg/kg bw/day based on an increase in methemoglobin and an increase in hepatic hemosiderin deposits from the 52-week dog study.
Lowest relevant oral NOAEL / LOAEL	NOAELacute: 8.3 mg/kg/day (28-day dog study) NOAELmedium-term: 0.5 mg/kg/day (13 week point of 52 week dog study) NOAELchronic: 0.5 mg/kg/day (52 week dog study)
Lowest relevant dermal NOAEL / LOAEL	> 1000 mg/kg/day (21 day rat study).
Lowest relevant inhalation NOAEL / LOAEL	No inhalation RDT studies were submitted

Genotoxicity	The genotoxic potential of hexaflumuron was investigated in three in vitro studies (Ames test, in vitro CA and CHO/HGPRT) and one in vivo study (MMN). The results of these tests were negative.

Carcinogenicity

Species/type of tumour	Hexaflumuron was tested for oncogenicity in two

	studies (rat, mouse). Tumour induction was negative for both species.
lowest dose with tumours	Not applicable

Reproductive toxicity

Species/ Reproduction target / critical effect	No treatment related effects on fertility were found on a 2-generation study (rat).
Lowest relevant reproductive NOAEL / LOAEL	Rat: NOAEL: 125 mg/kg bw/day NOAELF1parental: 5mg/kg bw/day based on hematopoietic toxicity effects.
Species/Developmental target / critical effect	Hexaflumuron didn't cause maternal toxicity or embriotoxicity in two teratogenicity studies (rat, rabbit).
Developmental toxicity	
Lowest relevant developmental NOAEL / LOAEL	Rat and rabbit: NOAEL>1000mg/kg bw/d

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	No treatment related neurological effects were found on an acute delayed neurotoxicity test in the domestic hen.
Lowest relevant developmental NOAEL / LOAEL.	NOAEL: 5000 mg/kg bw/d

Other toxicological studies

....	None

Medical data

....	None

Summary	Value	Study	Safety factor
Non-professional user			
ADI (acceptable daily intake, external long-term reference dose)	N/A	N/A	N/A
AOEL-S (Operator Exposure)	N/A	N/A	N/A
ARfD (acute reference dose)	N/A	N/A	N/A
Professional user			
Reference value for inhalation (proposed OEL)	N/A	N/A	N/A
Reference value for dermal/oral absorption concerning the active substance:			
AEL $_{short\text{-}term}$ (mg/kd bw/day)	0.08 mg/kg/day	28 day diet dog study	300
AEL $_{medium\text{-}term}$ (mg/kd bw/day)	0.005	13 week point in 53 week dog	100

	mg/kg/day	diet study	
AEL long-term (mg/kd bw/day)	0.005 mg/kg/day	52 week diet dog study	100
Reference value for dermal absorption concerning the representative product(s)[4]:	N/A	N/A	N/A

Acceptable exposure scenarios (including method of calculation)

Professional users	
Production of active substance:	N/A
Formulation of biocidal product	N/A
Intended uses	PT 18
Secondary exposure	
Non-professional users	N/A
Indirect exposure as a result of use	Adult accidental contact with bait

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 5, 10°C: DT_{50}= stable pH 5, 9°C: DT_{50}= stable pH 5, 25°C: DT_{50}= stable
	pH 7, 10°C: DT_{50}= not conducted pH 7, 9°C: DT_{50}= not conducted pH 7, 25°C: DT_{50}= 270 days
	pH 9, 10°C: DT_{50}= not conducted pH 9, 9°C: DT_{50}= not conducted pH 9, 25°C: DT_{50}= 22 days
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Direct photolysis (pH 5): DT_{50}= ca. 6.3days Indirect photolysis (pH 8): DT_{50}= ca. 7 days (photolysis only) or 4.7 days (photolysis and hydrolysis), Therefore no appreciable difference from direct photolysis) Hexaflumuron will photolyze, with the resulting major component being CO_2 and the difluorobenzamide degradate and the hydroxyl-aniline degradate.
Readily biodegradable (yes/no)	No
Biodegradation in seawater	Hexaflumuron, as used in the RECRUTE Pro bait

	system, will not be used or released into marine environments.
Non-extractable residues	<10% of applied radioactivity
Distribution in water / sediment systems (active substance)	Exposure of hexaflumuron in RECRUTE Pro bait system to anaerobic aquatic conditions is unlikely.
Distribution in water / sediment systems (metabolites)	Lack of exposure of hexaflumuron will result in no exposure of metabolites to anaerobic aquatic conditions.

Route and rate of degradation in soil

Mineralization (aerobic)	up to 40% in the benzoyl-labeled hexaflumuron (17-24% in one study)
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50}=280 days; 12°C DT_{50} = 99 days: 25ºC DT_{50} = 190 days: 10ºC DT_{50} = 148 days: 20ºC
Field studies (state location, range or median with number of measurements)	Dissipation and accumulation study were not submitted.
Anaerobic degradation	Hexaflumuron, as used in the RECRUTE Pro bait system, will not be exposed to anaerobic conditions, and even if the RECRUTE Pro system is used around buildings housing animals, hexaflumuron will not be released into manure storage facilities.
Soil photolysis	Hexaflumuron, as used in the RECRUTE Pro bait system, will not be present on the soil surface, and therefore will not be subject to soil photolysis.
Non-extractable residues	In the aerobic soil metabolism study, bound radioactive residues increased throughout the incubation period, reaching 45-70% and 20-25% in the aniline-label and benzoyl-label, respectively, after 1 year.
Relevant metabolites - name and/or code, % of applied active ingredient (range and maximum)	Two degradates (phenylurea and phenylamine) were observed that exceeded 10% of applied radioactivity (AR). Both were observed only from the degradation of ^{14}C-aniline-hexaflumuron. Phenylurea never exceeded 11% AR in any soil while phenylamine reached a max 20% AR in the Castle Rising soil before declining.
Soil accumulation and plateau concentration	-/-

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	soil applied, Kd = 147-1326 mL/g (average 504 mL/g) Kdoc = 3096-41170 mL/g no

Fate and behaviour in air

Direct photolysis in air	Due to the low vapour pressure, and the rapid degradation in air, air photolysis studies were not conducted.
Quantum yield of direct photolysis	Study not conducted
Photo-oxidative degradation in air	Latitude: .... Season: .... DT_{50} ....
Volatilization	Atmospheric half-life: 6.1 hours, assuming a hydroxyl radical concentration of $1.5x10^6$ radicals/cm3. For a 12-hour daylight period, the half-life is 0.51 days.

Monitoring data, if available

Soil (indicate location and type of study)	none
Surface water (indicate location and type of study)	none
Ground water (indicate location and type of study)	none
Air (indicate location and type of study)	none

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Rainbow trout	96 h	LC_{50}	LC_{50} was higher than the highest concentration tested (> 489.78 µg/L)
Bluegill sunfish	96 h	LC_{50}	LC_{50} was greater than the highest concentration tested (>141.86 µg/L).
Invertebrates			

Daphnia magna	48 h static test	EC_{50} immobility	0.11 µg/L
Daphnia magna	21 d semi-static test	Survival, reproduction and growth	NOEC (adult survival) = 0.0029 µg/L NOEC (reproduction) = 0.0029 µg/L EC_{50} (reproduction) = 0.008 µg/L
Algae			
Selenastrum capricorneum	Cell density at 24, 48, 72 and 96h Biomass 0-72h	E_bC_{50} E_rC_{50}	>1.91mg/L >1.91mg/L
	Growth rate 0-72h	NOErC	>1.91mg/L
Microorganisms			
Inoculum - Activated sludge (waste water treatment plant)	3h	EC_{50} Respiration rate	>100mg/L

Effects on earthworms or other soil non-target organisms

Acute toxicity to ………………………………..	Soil exposure, 14d exposure EC/LC_{50}>>880mg a.i./kg dry soil.
Reproductive toxicity to ………………………..	No test performed

Effects on soil micro-organisms

Nitrogen mineralization	(60 days), two concentrations were tested - 0.2 mg/kg soil and 2 mg/kg soil. N-mineralization was unaffected by both treatments. No effects were noted.
Carbon mineralization	84 days), two concentrations were tested - 0.2 mg/kg soil and 2 mg/kg soil. No effects were noted.

Effects on terrestrial vertebrates

Acute toxicity to mammals	Study not performed

Acute toxicity to birds	Northern bobwhite, LD_{50} >2000mg/kg bw Mallard duck, LD_{50} >2000mg/kg bw
Dietary toxicity to birds	Northern bobwhite, LD_{50} >4786 mg a.i./kg feed (equivalent to 900 mg a.i./kg bw/d) Mallard duck, LD_{50} >5200 mg a.i./kg feed (equivalent to 1405.5 mg a.i./kg bw/d)
Reproductive toxicity to birds	Not performed

Effects on honeybees

Acute oral toxicity	48h, EC/LC_{50}>>100 µg/a.i./bee – non-toxic to bees
Acute contact toxicity	48h, EC/LC_{50}>>100 µg/a.i./bee – non-toxic to bees

Effects on other beneficial arthropods

Acute oral toxicity	No test performed
Acute contact toxicity	No test performed
Acute toxicity to ………………………………..	

Bioconcentration

Bioconcentration factor (BCF)	3783, 7667, and 5600 for edible tissue, non-edible parts, and whole fish, respectively
Depuration time (DT_{50}) (DT_{90})	6.5, 13.5, and 10.4 days in edibles, non-edibles, and whole fish, respectively
Level of metabolites (%) in organisms accounting for > 10 % of residues	None

Chapter 6: Other End Points

Appendix II: List of Intended Uses

Object and/or situation	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment			Re marks:
			Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	number min max	interval between applications (min)	g a.s./L min max	water L/m^2 min max	g a.s./m^2 min max	
Elimination of subterranean termites in structures and terrain	RECRUTE* Pro	Subterranean termites (*Reticulitermes species, Coptotermes species and Heterotemes species*).	Cellu-losic bait	0.5% w/w	Bait	The number of bait stations applied per structure or area depends on the extent of the attack and termite activity present. Bait stations are used only where activity or damage is seen or suspected. 100g	2 weeks Bait stations are only replenished if there has been sufficient consumption to warrant replacement.	Not applicable	Not appli-cable	Not appli-cable	The active ingredient Hexaflumuron will be presented as a 0.5% w/w cellulose bait to be used within the Sentri*Tech Colony Elimination System . Prior to installation of the bait stations, determination of the extent of damage and termite activity is made. Then bait stations are placed appropriately. Once termites start feeding baits are replaced on an as needs basis. New sites for placing bait stations can also be detected throughout the treatment period. The period of treatment can be up to 18-24 months from point of active baiting, depending on the number and size of colonies to be eliminated

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