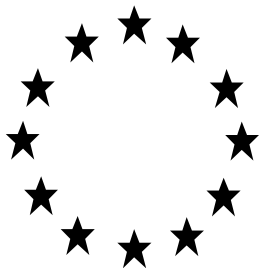
Directive 98/8/EC concerning the placing of biocidal products on the market

Inclusion of active substances in Annex I to Directive 98/8/EC

Assessment Report



CLOTHIANIDIN

Product-Type 8
(Wood Preservative)

13 September 2007

Annex I - Germany

Clothianidin (PT 8)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 13 September 2007 in view of its inclusion in Annex I to Directive 98/8/EC

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

This assessment report has been established as a result of the evaluation of clothianidin as product-type 8 (wood preservative), 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 a view to the possible inclusion of this substance into Annex I to the Directive.

Clothianidin (CAS no. 210880-92-5) was notified as an existing active substance, by Sumitomo Chemical Takeda Agro Company, Ltd., United Kingdom, hereafter referred to as the applicant, in product-type 8 (wood preservative).

Commission Regulation (EC) No 2032/2003 of 4 November 2003[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 5(2) of that Regulation, the Commission designated Germany 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 clothianidin as an active substance in product-type 8 was 28 March 2004, in accordance with Annex V of Regulation (EC) No 2032/2003.

On 25 March 2004, the German competent authority received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 25 June 2004.

On 30 November 2005, the Rapporteur Member State submitted, in accordance with the provisions of Article 10(5) and (7) of Regulation 2032/2003, 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 15 December 2005. The competent authority report included a recommendation for the inclusion of clothianidin in Annex I to the Directive for product-type 8.

In accordance with Article 12 of Regulation (EC) 2032/2003, the Commission made the competent authority report publicly available by electronic means on 28 March 2006. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

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

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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 OJ L 307, 24.11.2003, p. 1

On the basis of the final competent authority report, the Commission proposed the inclusion of clothianidin in Annex I to Directive 98/8/EC and consulted the Standing Committee on Biocidal Product on 13 September 2007.

In accordance with Article 11(4) of Regulation (EC) No 2032/2003, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 13 September 2007.

1.2. Purpose of the assessment report

This assessment report has been developed and finalised in support of the decision to include clothianidin in Annex I to Directive 98/8/EC for product-type 8. The aim of the assessment report is to facilitate the authorisation in Member States of individual biocidal products in product-type 8 that contain clothianidin. In their evaluation, Member States shall apply the provisions of Directive 98/8/EC, in particular the provisions of Article 5 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 the assessment report, which is available at the Commission website[3], shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Directive 98/8/EC, such conclusions may not be used to the benefit of another applicant, unless access to these data has been granted.

1.3. Overall conclusion in the context of Directive 98/8/EC

The overall conclusion from the evaluation is that it may be expected that products containing clothianidin for the product-type 8 will fulfil the requirements laid down in Article 10(1) and (2) of Directive 98/8/EC. This conclusion is however subject to:

i. compliance with the particular requirements in the following sections of this assessment report,

ii. the implementation of the provisions of Article 5(1) of Directive 98/8/EC, and

iii. the common principles laid down in Annex VI to Directive 98/8/EC.

Furthermore, these conclusions were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern

3 http://ec.europa.eu/comm/environment/biocides/index.htm

beyond those described will require an evaluation at Member State level in order to establish whether the proposed extensions of use will satisfy the requirements of Article 5(1) and of the common principles laid down in Annex VI to Directive 98/8/EC.

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

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

The identity of clothianidin (CAS No 210880-92-5) is given in detail in the confidential part of the dossier. The evaluation has established that for the active substance notified by Sumitomo Chemical Takeda Agro Company, none of the manufacturing impurities considered are, on the basis of information currently available, of toxicological or environmental concern.

Clothianidin belongs to the chemical class of chloronicotinyls/neonicotinoids and is a clear and colourless, solid powder. Its vapour pressure and volatility are very low. Clothianidin is a strong base and does not dissociate under acidic to slightly basic conditions. The water solubility is 0.327 g/L at 20 °C. The logPow of clothianidin is 0.7 at 25 °C. Hydrolysis only occurs at high pH and high temperature.

Clothianidin is thermally stable and does not form breakdown products while heating up to the melting point. Decomposition occurred above 200 °C. The compound is neither highly flammable (no relative self-ignition up to the melting point), explosive nor has oxidising properties. In conclusion, no hazard indication is required for the active substance. During storage of clothianidin in polyethylene bags for 24 months, no peeling, cracking or discoloration of the commercial packaging was observed and no swelling of the container walls occurred.

The identity of the representative wood preservative, which contains 0.1 % of the active substance clothianidin, is given in detail in the confidential part of the dossier. Due to the nature of the biocidal product (aqueous solution), the biocidal product is not expected to exhibit any hazardous physical-chemical properties

Analytical method for the active substance: Clothianidin was diluted in methanol and analysed directly by liquid chromatography (HPLC) using reversed phase conditions and UV detection, wavelength: 265 nm.

2.1.2. Intended Uses and Efficacy

Clothianidin has been evaluated for its use as a wood preservative belonging to product-type 8 according to Annex V of the directive 98/8/EC.

The participant envisaged the use classes 1 to 4 for the clothianidin containing wood preservative product. Evaluation of the submitted information resulted in the necessity to ask for additional data according to Article 10 (1) of Commission Regulation (EC) 2032/2003 in conjunction with Article 11(2) of Directive 98/8/EC to support the use class 4. As a consequence, the participant deleted the use class 4 from the label claim. Assessment of the clothianidin containing wood preservative product for application in the remaining use classes was found to be safe for use classes 1 and 2. Application in use class 3 indicated an

unacceptable risk for surface water, soil and groundwater. Therefore, appropriate risk mitigation measures are required to protect the environment.

The target organisms are insects (beetles and termites) on all kinds of construction wood, particle board and ply wood.

The intended uses for the representative biocidal product were foreseen only for industrial and professional application and are as follows:

1. Spraying or brushing (curative use; use classes 1-2) using a ready-for-use 0.1 % clothianidin containing formulation for remedial treatment of indoor wood. Spraying with low-medium pressure (4-7 bar) using electric or fuel driven pump and preservative reservoir.

2. Dipping treatment (preventive use; use classes 1-3) in industrial premises by water based application of water-based wood preservative via dipping/immersion process. Mechanical dipping in aqueous solution containing max. 0.0075 % clothianidin (max. 15 % of wood preservative concentrate containing 0.0 5% clothianidin). The retention for dipping treatment was estimated by the RMS and showed that 200 g /m² of a 0.0075 % solution yield 15 mg/m² clothianidin.

3. Vacuum pressure treatment (preventive use; use classes 1-3) in industrial premises by water based application of water-based wood preservative via vacuum pressure treatment. Aqueous application solution containing max. 0.002 % clothianidin (max. 4 % of wood preservative concentrate containing 0.05 % clothianidin). The retention that can be achieved depends on the treatment procedure, formulation and wood species, 20 kg/m³ of a concentrate containing 0,05 % clothianidin yield approximately 10 g/m³ clothianidin.

In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, and to apply adequately the provisions of Article 5(1) of Directive 98/8/EC and the common principles laid down in Annex VI of that Directive, the intended uses of the substance, as identified during the evaluation process, are also listed in Appendix II.

Efficacy:

Clothianidin belongs to the chemical class of insecticides known as neonicotinoids or chloronicotinyls and is especially active against homopteran and coleopteran pest species. The compound acts agonistically on insect nicotinic acetylcholine receptors located in the central nervous system (Nauen et al., 2001).

The insecticidal effect of clothianidin has been demonstrated by laboratory studies with larvae of the house longhorn beetle Hylotrupes bajulus as a species that represents wood destroying beetles and for the termite species Reticulitermes santonensis. The active ingredient was solubilised in ethanol and applied by pressure treatment to demonstrate the insecticidal effect and determine toxic values towards both test organisms.

The concentrations of clothianidin in the ethanolic test solution that were necessary to control Reticulitermes santonensis as well as Hylotrupes bajulus by vacuum impregnation were lower than the proposed maximum concentration. However, data regarding lower concentrations for certain products will be defined during product authorisation.

The submitted studies indicate preventive action of clothianidin against termites and beetles. The tests have been performed with the active substance clothianidin in ethanol. Tests that have been performed with a pilot product indicate a limited curative action of this product.

Water-based formulations containing 0.05 % clothianidin are proposed for dipping treatments and vacuum pressure treatment. Data on the preventive efficacy of such formulations are not reported.

Therefore, the label claim ‘preventive efficacy’ is not supported by the experimental data.

The dossier does not include data that describe the efficacy of clothianidin after surface treatments.

In the frame of product evaluation, additional data have to be provided to support the complete requested label claim of the product (see chapter 3.3).

Overall, it could be demonstrated, that clothianidin and a clothianidin containing formulation have shown efficacy against insects, and therefore the inclusion into Annex I of Directive 98/8/EC can be recommended.

2.1.3. Classification and Labelling

Up to now there is no legal classification, because clothianidin has not been inserted into Annex I of Directive 67/548/EEC yet. Evaluation of the submitted data under Directive 98/8/EEC resulted in the following proposal for classification and labelling:

Table 2-1 Proposed classification

Classification	**As proposed by the RMS:**	
Class of danger	Xn	Harmful
	N	Dangerous to the environment
R phrases	R22	Harmful if swallowed
	R50	Very toxic to aquatic organisms
	R53	May cause long-term adverse effects in the aquatic environment
S phrases	*S2*	*Keep out of the reach of children*
	S13	*Keep away from food, drink and animal feedingstuffs*
	S46	*If swallowed, seek medical advice immediately and show this container of label*
	S60	This material and/or its container must be disposed of as hazardous waste
	S61	Avoid release to the environment. Refer to special instructions/ material safety data sheet

<u>Remark:</u> S-Phrases in italics are optional. S2-13-46 are thought to be used for substances, which are used by the general public.

In deviation to the participant's classification and labelling of clothianidin, a classification and labelling proposal regarding the environmental hazard was generated. This proposal based on the 48h-LC50 value of 0.029 mg/l for *Chironomus riparius*. Although this species is not a standard test organism for classification purposes, this LC50 value was chosen due to the specific toxicity of clothianidin to insects. The following safety phrases are mandatory for labelling: "This material and/or its container must be disposed of as hazardous waste"; "Avoid release to the environment. Refer to special instructions/ material safety data sheet".

Within the Annex I inclusion of clothianidin under the plant protection product Directive 91/414/EEC the same classification was proposed.

The proposed classification of clothianidin, given in table 2-1 should be discussed further at the EU Technical Committee on Classification & Labelling.

The participant submitted data for a wood protection product with a preliminary trade name. However, this product has not been placed on the market yet. The classification and labelling of the representative biocidal product was done in compliance with the requirements of

Directive 1999/45/EG. Two substances of the biocidal product are identified as hazardous for the environment. The concentration of both substances is below the concentration limit that triggers the classification of the preparation. The available ecotoxicological studies with the preparation show an effect value of < 10 mg/l for green algae that would imply the classification N, R 51. Concerning biodegradation and bioaccumulation, apart from the surface activity of the co-formulant in the product, there are no indications for classifying the product as R 53 based on the Directive 1999/45/EEC.

As the classification N, R51 could not stand for its own and has to be connected with the risk phrase R 53, that could not be applied in this case, our proposal is not to classify the representative biocidal product as dangerous for the environment.

Table 2-2 Proposed classification of the representative biocidal product

Classification according Directive 1999/45/EC	**As proposed by the RMS:**	
Indication of danger		Not required.
R phrases	None	None
S phrases	None	None

Proposed packaging and labelling (recommended by the RMS)

Proposal for safety-data sheet (where appropriate):

The proposal for the safety data sheet as given by the participant is not acceptable due to the fact that some of the contents do not reflect all information provided in the dossier. As the biocidal product in question is not placed on the market yet the necessary information in the safety data sheet has to be provided for the authorisation process of biocidal products containing clothianidin as an active substance. Additional information according to Art. 20 (3) of the directive: As no label, packaging or leaflet for the representative biocidal product is provided by the participant obviously none of the additional information according to Art. 20 (3) can be evaluated here. This is acceptable as the representative biocidal product is not placed on the market yet. The necessary elements of labelling and packaging have to be provided for the authorisation process of biocidal products containing clothianidin as an active substance.

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification

Absorption, distribution, excretion, and metabolism

Clothianidin is rapidly and almost completely absorbed in rats after oral application essentially independent of dose level (although high dose levels have been found to saturate the absorption process), pre-treatment and label position. Distribution occurs rapidly to all tissues with excretory organs (liver, kidney, urinary bladder) and nasal mucosa displaying higher levels than blood within one hour after dosing. Excretion proceeds mainly via urine and is about 90% at low doses by 24 hours post dose. No potential for accumulation was found. Clothianidin was the major fraction in excreta with females metabolising a smaller fraction than males. In total, 13 metabolites were identified (TZNG and MNG ≥10%, MTCA ~8.5%, NTG ~4% of applied dose). A dermal absorption of 2 % was derived from a study in male rhesus monkeys conducted with a plant protection product.

Acute toxicity

Clothianidin exhibits moderate acute oral toxicity ($523 < LD_{50} < 1216$ mg/kg bw for female rats Lethality was not observed when tested by the dermal route or when inhaled as a liquid aerosol. Clinical signs were similar after oral and inhalation exposure. No dermal and no ocular irritation were noted after application of clothianidin to the skin and eye of rabbits. Clothianidin did not display skin sensitisation potential in a guinea pig maximisation test according to Magnusson and Kligman.

Medium-term toxicity

Main effects of repeated oral administration of clothianidin in all tested species were a reduction in body weight gain and frequently reduced food consumption compared to the control. Effects on WBC and RBC parameters were observed at doses inducing body weight suppression in rodents and to a lower extent in dogs. In the rat, a mild induction of CYP450 enzymes of the liver was reported in a 90-d study with incomplete recovery. Effects on the intestinal tract in dogs as well as reduced kidney weight combined with an increase of inorganic phosphorus are considered to be substance-related effects.

The oral NOAEL in rats was 500 ppm (27.9 mg/kg bw/d) for males based on reduced body weight, body weight gain, increase of enzyme activity in the liver and pigmentation of the spleen at 3000 ppm (202.0 mg/kg bw/d) in the 90-d study. The dermal NOAEL in rats was > 1000 mg/kg bw/d for males and females, based on the results of a 28-d study.

The oral NOAEL in mice was 500 ppm (82 mg/kg bw/d) for males, based on a decrease in body weight gain and food conversion at 1000 ppm (160 mg/kg bw/d) in the 90-d study. In this as well as in the 28-d study, treated mice, especially males, displayed an increased mortality when subjected to a light ether narcosis for blood sampling.

The oral NOAEL in dogs was 650 ppm (19.3 mg/kg bw/d), based on a decrease of WBC parameters (males) and protein (females) at 1500 ppm (40.9 mg/kg bw/d) in the 90-d study.

Genotoxicity

Based on the results of in vitro and in vivo genotoxicity tests, clothianidin is unlikely to pose a genotoxic risk to humans.

Chronic toxicity/ Carcinogenicity

The NOAEL in rats was 150 ppm (9.7 mg/kg bw/d), based on interstitial cell hyperplasia of the ovaries at 500 ppm (32.5 mg/kg bw/d) in females in the 104-wk study.

The NOAEL in mice was 350 ppm (47.2 mg/kg bw/d), based on reduced body weight development (females), behavioural changes (vocalisation) and hepatocellular hypertrophy at 1250 ppm (171 mg/kg bw/d) in the 78-wk study.

Clothianidin is unlikely to pose a carcinogenic risk to humans.

Reproduction toxicity

In all developmental toxicity studies, effects on the conceptus were observed at dose levels which also induced toxicity in the parent animals. No special sensitivity of developing organisms to clothianidin was identified. Up to a dose level of 125 mg/kg bw/d during day 6-19 of pregnancy which reduced food consumption and body weight development in dams, clothianidin did not affect the pregnancy rate, litter parameters or external, skeletal and visceral changes of foetuses in rats. In rabbits, abnormalities in foetal lung lobation as well as premature births or abortions were observed at doses of 75 and 100 mg/kg bw/d, which also induced maternal toxicity (mortality, decreased body weight gain).

In a rat two-generation study, effects on the parent generations (P, F1) included reduced body weight gain during the pre-mating period, pregnancy and lactation as well as reduced thymus weights and a decrease in sperm (progressive) motility at a dose level of 2500 ppm. The changes had no adverse effects on the fertility of these animals. However, because of the difference in sperm parameters between rodents and humans and because of a possible mechanistic link between nACh receptors and sperm motility, the dose level of 2500 ppm is considered the LOAEL with respect to fertility effects. F1 and F2 offspring at 2500 ppm were found to have decreased viability in the perinatal period (stillbirths, early postnatal deaths), lower body weights at birth, reduced body weight gain during the postnatal period, slightly delayed puberty and reduction in absolute and relative spleen weights at weaning.

The NOAEL for offspring toxicity was 150 ppm (10 mg/kg bw/d), based on a delay of preputial gland development at 500 ppm in the F1 generation. There were no obvious antiandrogenic or oestrogenic effects in adult males or females and anogenital distance in newborn F2 pups was not affected by clothianidin exposure of the dams. As this makes it unlikely that the effect is elicited in utero through interference with androgen production or signaling the effect on male sexual maturation is not considered relevant to derive any reference doses for adults.

Clothianidin is unlikely to pose a teratogenic risk to humans at doses below those inducing toxic effects in the mother. Clothianidin is also unlikely to affect fertility and developmental parameters in humans at doses below a range that elicits other toxic effects in adults. However, although prepubertal males will not be exposed at the workplace this developmental NOAEL is perceived relevant for secondary exposure through treated products.

Neurotoxicity

In adult rats, transient neurobehavioural effects were observed after acute oral administration of clothianidin, which are considered to be neurobehavioural evidence of systemic toxicity and/or signs of pharmacological overstimulation, but not indications for specific neurotoxicity. No relevant treatment-related effects were seen in the FOB, motor activity assessments or histopathological examinations of nervous or muscle tissues in a 90-d neurotoxicity study. There was some indication for developmental neurotoxicity in rats at doses which also induced reductions of maternal and offspring pre-weaning body weight gain and a slight decrease of offspring viability after weaning. Female offspring exhibited reduced motor activity on post-natal day 62 which, in the absence of exposure to the test substance at the time of testing, could indicate residual neurodevelopmental changes.

The studies identified an acute neurotoxicity NOAEL of 60 mg/kg bw for males and 100 mg/kg bw for females. The subchronic neurotoxicity NOAEL was 177 mg/kg bw/day in males, 200 mg/kg bw/day in females and the NOAEL for developmental neurotoxicity 42.9 mg/kg bw/day.

Other studies

An oral single dose study used mice and rats for various endpoints of pharmacological relevance. Mice proved to be the more sensitive species. The overall NOAEL was 25 mg/kg bw, based on clinical signs. The convulsions following sub-threshold electroshock at ≥ 25 mg/kg bw were not considered relevant for human risk assessment, because this result was derived from a highly artificial testing scenario not normally used in toxicity studies.

The metabolites tested (MNG, TZNG, TMG, TZMU, MG), with the exception of TMG and MG, showed a similar or lower acute oral toxicity than the parent compound. The LD_{50} values for MG and TMG in the rat were in the range between 450 and 570 mg/kg bw, below those observed for clothianidin. None of these metabolites was considered positive in the bacterial reverse mutation test.

Medical data

No medical reports on the manufacturing personnel have been submitted.

2.2.1.2. Effects assessment

The most critical endpoints for acute toxicity were established from the results of a pharmacological study performed with clothianidin and a NOAEL of 25 mg/kg bw was derived. Applying an Assessment Factor of 100, the acute systemic acceptable exposure level (AEL_{acute}) results in a value of 0.25 mg/kg bw (oral absorption > 90 %).

Medium-term oral toxicity studies in dogs, mice and rats resulted in similar no-observed-adverse effect levels. The derivation of the overall NOAEL of 20 mg/kg bw/d is supported by the NOAEL for maternal toxicity from the developmental toxicity study in rabbits. Applying an Assessment Factor of 100, the medium-term systemic acceptable exposure level ($AEL_{medium-term}$) results in a value of 0.2 mg/kg bw/d (oral absorption > 90 %).

The 2-year study in rats was selected as the most relevant study for long-term exposure calculations.

The NOAEL of 10 mg/kg bw/d derived from this study is supported by the overall NOAEL from the 2-generation study in rats. Applying an Assessment Factor of 100, the long-term systemic acceptable exposure level ($AEL_{long-term}$) results in a value of 0.1 mg/kg bw/d (oral absorption > 90 %).

An ARfD and an ADI should not be derived for clothainidin used in wood protection products (PT 8) since no residues in food or feed are expected.

A dermal absorption of 2 % was derived from a study in rhesus monkeys conducted with a similar product.

In the absence of data, an inhalative absorption of 100 % is assumed.

The representative wood protection product containing 0.1 % clothianidin is considered to be non-toxic if swallowed or applied to the skin. An acute inhalation study has not been submitted. This was accepted in connection with clothianidin's inclusion into Annex I of Directive 98/8/EC.
The representative wood preservative is not irritating to the skin or to the eye. Furthermore, there is no evidence for any skin-sensitising potential.

2.2.1.3. Exposure assessment

Exposure of professionals

Clothianidin is produced in Japan and is imported to the EU as a powdery solid. Different aqueous solutions with a maximum content of 0.1 % active substance are formulated for uses as biocidal products in curative and preventive wood protection. For the assessment of inhalative exposure, the main focus is set on the exposure to dusts and droplet aerosols. Due to the low vapour pressure (vapour pressure of 1.3×10^{-10} Pa, 25°C), inhalative exposure to vapour is of minor relevance. Also the assessment of dermal exposure is influenced by the exposure to dusts and aerosols mostly. The following scenarios are covered by the exposure assessment in this report:

- Formulation of the biocidal product
- Curative treatment with ready-for-use formulations containing 0.1% active substance:
    - Spraying (indoor, 4-7 bar, 80 min/day)

- Brushing

- Preventive treatment with 0.05 % active substance:

- Vacuum pressure process (the biocidal product is diluted for application to an aqueous solution containing 0.002 % of the active substance, 2 cycles per day)

- Dipping/immersion (the biocidal product is diluted for application to an aqueous solution containing 0.0075 % of the active substance, 5 cycles per day)

- Secondary exposure:

- Mechanical processing of treated wood (secondary exposure to wood dust of treated wood and residues in treated wood)

Potential exposure estimates concerning formulation and use of the representative biocidal product are performed which do not take account of safety measures. From the content of the active substance clothianidin a total internal dose for professionals is calculated assuming 2 % dermal absorption and 100 % inhalative absorption. In all exposure scenarios skin contact significantly contributes to the total internal dose. The highest estimate results in an internal dose of 4.4 mg clothianidin/person/day for indoor spraying (scenario 3).

To give an example the exposure assessment for this scenario is described in more detail (an overview of all assessed scenarios is given in table 2-3 below)

In scenario 3 occupational exposure for curative treatment by spraying under roof is assessed. During spraying droplet aerosols are formed and inhalative and dermal exposure may occur. The mixing & loading and post-application phase do not significantly contribute to the total exposure. The direction of spraying under roof will be mostly overhead, thus leading to exposure levels at the upper end of the data range obtained with Model 2 (Spraying) of the TNsG Human Exposure to Biocidal Products (Part 2, p. 146-148). Taking into account the concentration of 0.1 % active substance and the duration of 80 minutes per day the resulting inhalation exposure is calculated as a shift average to **0.03 mg/m^3**. The potential dermal exposure of hands, body and feet is estimated to be **203 mg/person/day** of clothianidin. In summary an internal dose of **0.3 mg/person/day** results from inhalation (100 % of 0.03 mg/m^3 x 10 m^3) and an internal dose of **4.1 mg/person/day** from dermal contact (2% of 203 mg/person/day).

<u>Exposure of non-professionals</u>

Non-professional use of the representative biocidal product is not intended, preventive as well as curative applications of the wood preservative are restricted to professional operators, so that primary non-occupational exposure can be excluded. A secondary exposure of non-professionals resulting from production process of the active substance or the biocidal product or resulting from application of the wood protection product is not anticipated for in all scenarios mentioned and bystanders will not have access. Acute secondary exposure to clothianidin by contact to curatively treated wood can be ruled out since mechanical processing of load-bearing wood components is strictly forbidden for laymen. However, acute secondary

exposure to clothianidin by contact to preventively treated wood has to be taken in account, since absorption during use of treated wood (e.g. inhalation by sanding) by adults or oral ingestion by infants chewing treated wood is likely. Beyond this, possible secondary exposure to clothianidin-containing wood protection products could be chronic resulting from inhalation of volatilised residues or ingestion of/dermal exposure to dislodged surface residues from treated surfaces.

2.2.1.4. Risk characterisation

Professionals risk assessment

As repeated exposure at the workplace with a long-term characteristic cannot be excluded, occupational risk assessment uses the **internal long-term reference dose** expressed as **7.0 mg/person/day** (0.1 mg/kg/day x 70 kg) for a rough but cautious assessment to decide on concern (table 2-3)4. In all cases professional exposure is below the reference dose for the in table 2-3 listed specific conditions. Because of the precautionary elements in the assessment it is concluded that risks at the workplace are low. The general legislation on occupational safety and health is sufficient to control workplace exposure. As support two additional specifications are proposed concerning the use of clothianidin and its products (see occupational safety measures, chapter 3.5)

4 The risk characterisation for professionals is based on a standard body weight of 70kg. The use of a 60 kg body weight will not change the outcome of the risk characterisation. For the product authorisation the value of 60 kg should be used.

Table 2-3: Risk characterisation for professionals using Tier 1

Exposure scenario		Specific conditions	potential exposure (external values)		Total potential internal dose (mg/person/day) (1)	% long term reference dose(2)
			inhalation (mg/m^3)	dermal (mg/pers/d)		
2.	**Formulation of biocidal product to 0.1% aqueous solution**	Weighing and controlling of the dosage procedure (LEV present), duration: 15 min., frequency: daily Filling of the liquid biocidal product (0.1 % active substance) into 1000 l containers, duration: 150 min., frequency: daily	0.2	85	3.7	53 %
3.	**Spraying**	Conc. biocidal product 0.1 % , spray pressure: 4-7 bar, indoor use, direction: overhead, duration: 80 min., frequency: 3 days a week	0.03	203.5	4.4	63 %
4.	**Brushing**	Conc. biocidal product 0.1 %, direction: level, duration: 8 h, frequency: 3 days a week	negligible	47	0.9	13 %
5.	**Vacuum pressure process**	Conc. biocidal product 0.05 %, the biocidal product is diluted for application to an aqueous solution containing 0.002 % of the active substance, duration: 2 cycles per day, frequency: daily	2.9×10^{-5}	6.0	0.1	1.4 %
6.	**Dipping/Immersion**	Conc. biocidal product 0.05 %, the biocidal product is diluted for application to an aqueous solution containing 0.0075 % of the active substance, duration: 5 cycles per day, frequency: daily	negligible	10.7	0.2	2.8 %
7.	**Mechanical processing of treated wood**	Sawing/sanding of treated wood (inhalation) Wiping residues (dermal)	0.0004	0.16	0.16	2.3 %

(1) 100% inhalative absorption, breathing volume of 10 m^3 per shift - 2% systemic availability after dermal exposure

(2) 0.1 mg/kg/d ($AEL_{long\text{-}term}$) x 70 kg/person

Conclusion

As can be seen from table 2-3, for the professional exposure scenarios evaluated the total potential internal dose is below the long term reference dose. Since there are several precautionary elements in the Tier 1 assessment it can be concluded that occupational risks in the scenarios evaluated are low and do not need further action even though protection measures at the workplace are not yet taken into account.

Non-occupational risk assessment

The intended use of the representative biocidal product was foreseen only for trained professionals. Thus, a risk characterisation for non-professional users (primary exposure) is not relevant. Moreover, no secondary exposure of non-professionals is anticipated during production of the active substance or the formulation process of the biocidal product. During spraying/brushing and subsequent drying of the wood no secondary exposure of bystanders will occur either, if the application area is closed off for bystanders.

Chronic possible exposure of occupants of houses to clothianidin (curative treatment scenario) is considered negligible by inhalation but resulted in an estimated totally absorbed dose of clothianidin through the skin and by oral uptake making up **1.0 % of AEL**$_{\text{medium-term}}$ (0.2 mg/kg bw/d) in the case of adults or **71.5 % of AEL**$_{\text{medium-term}}$ in the case of infants, respectively. Calculations fully cover conditions of potential secondary dermal exposure in the preventive treatment scenario because the application rate of clothianidin is nearly two orders of magnitude lower than in the case of curative treatment. Acute possible exposure of non-professionals is 8 and 4 orders of magnitude lower than the AEL$_{\text{acute}}$ for adults and infants, respectively.

Taking all together, the use of the submitted representative biocidal product will bear no undue risk for bystanders for intended uses if above mentioned prerequisites, e. g. bystanders will not be allowed to enter the spraying area during application, are fulfilled. The general public will not be exposed to clothianidin in its regular use as a wood preservative.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Biodegradation

Clothianidin is not readily biodegradable. In a water/sediment system partial degradation in biologically active systems was observed. However, primary degradation of clothianidin in the water phase and in the entire systems is slow. Taken into account the three assessment-relevant parameters primary and ultimate degradation together with the extent of bound residues in the sediment, clothianidin must be considered to be persistent in aquatic systems.

From soil laboratory studies the $DT_{50,\ 20\ C}$ values determined varied between 143 and > 1 year (271 – > 1 year converted to 12^{o}C average EU Outdoor temperature) and mineralisation of clothianidin was found to be low to negligible. Four metabolites were detected in the soil extracts: MNG (N-methyl-N'-nitroguanidine) and TZNG (N-(2-chloro-5-thiazolylmethyl)-N'-

nitroguanidine) besides TZMU (N-(2-chlorothiazol-5-ylmethyl)-N'-methylurea) and NTG (Nitroguanidine) as minor metabolites. Only MNG is predominant with 10.7 %. In the overall assessment of laboratory studies on aerobic biodegradation in soil, clothianidin is categorised as persistent in soil. The measured DT_{50} values for the metabolites MNG are 82 – 108 days and 62 – 111days for TZNG respectively.

Recalculation of DT_{50}-values due to FOCUS-kinetics results in a DT_{50}-value of 274 d (20°C). Transformation to an average EU outdoor temperature of 12 °C leads to a DT_{50}-value of 515 d. Thus confirming the insignificant primary degradation and the high persistency of clothianidin as already demonstrated in the laboratory studies. In both bare and cropped soils, translocation of clothianidin into deeper soil layers than 10-20 cm can be excluded down to a concentration of 2 µg/kg. All concentrations of MNG and TZNG in deeper soil layers than 0-10 cm were below the limit of detection of 2 µg/kg.

Abiotic degradation

Clothianidin was stable to hydrolysis in sterile buffer solutions at pH 4, 5, and 7, but degrades slowly at pH 9. No transformation products were identified at pH 5 and 7. Minor transformation products at pH 9 were CTNU (N-(2-chlorothiazol-5-ylmethyl)-N'-nitrourea), TZMU (N-(2-chlorothiazol-5-ylmethyl)-N'-methylurea), and ACT•HCl (2-chlorothiazol-5-ylmethylamine hydrochloride). The latter seems to be the final transformation product.

Solar radiation will lead to a rapid photolytic degradation of clothianidin in aquatic systems under experimental conditions. However, the transferability of the degradation rates to environmental conditions is rather limited.

Based on the half life and chemical lifetime of clothianidin in the atmosphere, accumulation in the air is not to be expected.

Distribution

The adsorption and desorption laboratory studies indicated that clothianidin could be classified as being medium to highly mobile in soil. The major soil metabolite MNG was classified as being very highly mobile whereas TZNG was found to be moderately mobile. These results indicate that the parent compound and the major transformation products (MNG, TZNG) have medium to very high potential for leaching. However, this was not confirmed in lysimeter and biodegradation field studies.

Mobility

In neither of the two lysimeter studies performed for the use of the active substance as plant protection product the parent compound occurred in the leachates. The main metabolite MNG remained below 0.1 µg/L as well as the other metabolites. Neither the parent nor MNG and TZNG could be detected in deeper soil layers in the lysimeter studies. Thus, under the given test design for agricultural soils a contamination of groundwater by clothianidin appears to be of less relevance.

Bioaccumulation

The low P_{ow} indicates that clothianidin has low potential to bioaccumulate in organisms. Both estimated bioconcentration factors for the aquatic (BCF_{fish} = 0.78) and the terrestrial compartment ($BCF_{earthworm}$ = 0.9) can be classified as low.

2.2.2.2. Effects assessment

Aquatic compartment

Clothianidin is of low acute toxicity to fish (96h-LC_{50} > 100 mg/L) and only slightly toxic to daphnids (48h-EC_{50} = 26 mg/L[‡]) and green algae (96h-E_bC_{50} = 55 mg/L; 96h-E_rC_{50} > 120 mg/L). However, due to the mode of action, the toxicity to aquatic insects is high. The lowest effect value in a long-term laboratory study was obtained for the midge *Chironomus riparius* (28d-EC_{10} = 0.65 µg/L). Also in a mesososm study freshwater insects were found to be highly affected by the substance (NOEC = 1 µg/L). A $PNEC_{water}$ of 0.13 µg/L was derived from the available studies.

For the representative biocidal product containing 0.1 % clothianidin, short-term tests with fish, daphnia and green algae are available. The LC/EC_{50} values for fish and daphnia were > 100 mg/L. For green algae an ErC_{50} of 5.17 mg/L was obtained that is below the effect value for the active substance. This might be caused by another component of the biocidal product. The relevant effect value for the active substance is however from a long-term study with the midge *Chironomus riparius*. The very low effect value obtained for this species is caused by the specific mode of action of clothianidin to insects. Therefore, it is not expected that with the product a higher toxicity to this species can be found caused by any of the other components in the biocidal product. In conclusion, the $PNEC_{water}$ for the active substance clothianidin is also appropriate to assess the effects of the active substance clothianidin in the biocidal product.

Sediment

Studies in which the test organisms were exposed to clothianidin via spiked sediment are not available. Therefore, the $PNEC_{sediment}$ was derived from the $PNEC_{water}$ using the equilibrium partitioning method, resulting in a $PNEC_{sediment}$ of 0.55 µg/kg ww.

Terrestrial compartment

Tests with earthworms, collembolans, plants and soil microorganisms have been provided. The lowest effect value was obtained in an earthworm reproduction study (56d-NOEC (reproduction) = 0.1 mg/kg dw). In addition, there is published information on the toxicity of clothianidin to terrestrial arthropods. This information points to a higher sensitivity of certain terrestrial arthropods (*Poecilus cupreus*: 77d-NOEC (mortality) = 0.02 mg/kg dw). A $PNEC_{soil}$ of 1.8 µg/kg ww was derived from the available data. No data have been submitted on the

‡ *in the evaluation of the same test under PPPD 91/414/EC an EC_{50} of 40 mg/L was derived. However 70 % effect was reported at 32 mg/L test concentration. Therefore a recalculation of the EC_{50} value was performed resulting in an EC_{50} of 26 mg/L.*

effects of the biocidal product to terrestrial organisms. Therefore, the above derived $PNEC_{soil}$ is also used to assess the effects of the active substance clothianidin in the biocidal product. However, it has to be taken into account that there is no information how the other components in the biocidal product may contribute to or influence the toxicity of clothianidin to terrestrial organisms.

2.2.2.3. Exposure assessment

For the life cycle stage "production" no exposure assessment has been performed as the active substance is produced outside of the EU.

For the life cycle stage "formulation of the biocidal product" no exposure assessment has been performed as the applicant stated no emissions to the environment during formulating of the biocidal product. Applicant's statement is deemed to be plausible.

No exposure estimation has been performed for the life cycle stages "professional" and "private use of the biocidal product" as

- professional use is intended for use classes 1 and 2 (indoor use) assuming negligible emissions to the environment and
- private use of clothianidin-based wood preservatives is not intended by the applicant.

Predicted environmental concentrations (PECs) have been estimated for two life cycle steps: the industrial use of clothianidin-based wood preservatives and the service life of the pre-treated timber. The applicant applied for an intended use of pre-treated timber (preventive) for use classes 1 – 3. The emissions for industrial use and the service life have been estimated using the guidance given in the OECD Emission Scenario Document for Wood Preservatives (2003) and the EU Technical Guidance Document on Risk Assessment (2003).

The environmental exposure estimation of the active substance in the life cycle stage "industrial use" comprises the exposure estimation for the industrial application of the biocidal product including the post-treatment conditioning and for the industrial storage of the treated wood prior to shipment. Two application techniques have been considered: Dipping process and vacuum pressure treatment. For estimation of emissions from on-site storage of treated timber different emission scenarios were identified. In the standard scenario (scenario A) direct losses to the terrestrial compartment were postulated, suggesting that one half of the leachate runs directly to surface water, where the other half seeps completely into the storage site soil. The other scenarios follow the assumption that the timber treated on industrial site is stored on hard standing (concrete ceiling, asphalt covering) and that the whole fraction of rainwater from run-off of the storage site directly enters the surface water (scenario B) or the whole leachate run-off will enter a sewage treatment plant via facility drains prior to the release to the surface water (scenario C).

For "wood in service" the emission scenarios "Fence", "House" and "Noise barrier" have been estimated.

Two different time windows have been considered for the exposure assessment. TIME 1 reflects to the initial assessment period and covers a period of 30 days. The longer time span (TIME 2) for wood during storage has been fixed to 20 years whereas for service life TIME 2 is related to the application process (dipping/immersion = 15 years; pressure treatment = 20 years).

2.2.2.4. Risk characterisation

Aquatic compartment

There is no risk to sewage treatment plants from industrial application, storage, and wood in service.

For surface waters industrial application by dipping and vacuum pressure treatment resulted in PEC/PNEC ratios lower than 1.

For storage of pre-treated timber after dipping and immersion a risk for surface water was identified. In case of 50% run off (scenarios A) as well in the case of 100% run off (scenario B) from the storage place the PEC/PNEC ratios are above one. In case that the 100% run-off from sealed flooring enters a STP via the facility drain (scenario C) the trigger value for surface water is also exceeded for both application methods.

For wood in service the only scenario considered for the aquatic compartment is the noise barrier. The calculated PEC/PNEC ratios indicate no risk to the environment.

As a risk refinement is not possible appropriate risk reduction measures are recommended during storage of pre-treated timber.

Terrestrial compartment including groundwater

For the two industrial application techniques investigated the PEC/PNEC ratios for soil and groundwater pose no risk to the terrestrial compartment.

For treated timber held in storage, the estimated PEC/PNEC ratios for soil (50 % scenario) after dipping (19) and pressure treatment (6) indicate a risk. The hazard profile of clothianidin has shown that it has to be categorised as highly persistent in soil. Continuous emissions to soil during storage of clothianidin-treated timber resulted also in unacceptable PEC/PNEC values to groundwater (44 - 132) applying a worst case estimation scenario. Therefore, appropriate risk mitigation measures must be applied for pre-treated timber held in storage. These measures would be effective to both environmental compartments soil and groundwater.

The best way to be sufficiently protective of the environment would be to keep the treated timber on storage places covered by roofs. As this measure is not a standard practice to industrial sites further options should be taken into consideration. Alternatively storage of pre-treated timber should be carried out on areas of hard standing exhibiting impermeable grounds. As described above (see subchapter Aquatic compartment) this measure will be not sufficient protective to surface water during storage of treated timber by dipping. In order to protect surface water the leachate run-off must be collected and recycled into the impregnation

process. In addition, feasible waste treatment options have to be proven when recycling to the impregnation tank is not practicable. During on-site storage of pre-treated timber several risk mitigation processes have to be applied to confirm that clothianidin presents no unacceptable risk to the aquatic and terrestrial compartment.

The risk assessment for all relevant wood in service scenarios conducted lead to unacceptable PEC/PNEC ratios to the terrestrial compartment. The estimated PEC/PNEC values for soil were in the range of 6 to 32 for the dipping process and between 2 and 21 for the vacuum pressure process, respectively.

In view of the risk identified for the soil compartment, appropriate risk mitigation measures have to be taken to protect that compartment. For the risk characterisation only data from a pilot-product on ethanol basis were available. When assessing ready for use products containing the active substance together with fixatives and additives it is important to reassess the emission behaviour via experimental leaching tests.

At present there are no appropriate risk mitigation measures for wood in service (use class 3) available. The so far discussed alternative “top coating” is only appropriate if the wooden structure does not significantly change its dimensions which will inevitable occur if permanently exposed to weathering. Furthermore, a top coating will not persist for a longer time span (3-5 years) preventing losses of biocides to the environment. Consequently, the assessment of a given wood preservative containing clothianidin should include experimental data of any risk mitigations proposed e.g. top coating to base the risk characterisation on solid grounds.

PBT Assessment

Clothianidin does not fulfil the PBT criteria as the substance does not bioaccumulate although it is very persistent and toxic.

2.2.3. Listing of endpoints

In order to facilitate the work of Member States in granting or reviewing authorisations, and to apply adequately the provisions of Article 5(1) of Directive 98/8/EC and the common principles laid down in Annex VI of that Directive, the most important endpoints, as identified during the evaluation process, are listed in Appendix I.

3. DECISION

3.1. Background to the Decision

Article 10 of the Biocides Directive 98/8/EC addresses the inclusion of an active substance in the Annexes I, IA or IB. For the decision of inclusion or non-inclusion, it has to be examined if the criteria of article 10 (1) are fulfilled.

As the participant stated in his dossier the representative biocidal product, which contains the active substance clothianidin is not placed on the market, yet. This formulation is a “pilot product”, on which further development will be necessary. This will also open the eventuality to change the product composition. However, it will be part of the product authorisation process to evaluate the “final” biocidal product regarding its potential to cause a risk for human, animals, and the environment.

The physico-chemical properties of the clothianidin containing wood preservative product are deemed acceptable for the appropriate use, storage and transportation of the biocidal product.

Efficacy tests, which have been performed with the active substance clothianidin in ethanol indicate preventive action of clothianidin against termites and beetles. Testing of the representative wood preservative indicates a limited curative action of this product and at present no statement of the preventive efficacy of the biocidal product is possible. Overall, it could be demonstrated, that clothianidin and a clothianidin containing formulation have shown efficacy against insects, and therefore the inclusion into Annex I of Directive 98/8/EC can be recommended.

Nevertheless, additional data have to be provided for the wood preservative to support the complete requested label claim of the product (see chapter 3.3).

The estimation of hazards and the exposure assessment for human health for the representative biocidal product showed the following results: The biocidal product is non-toxic if swallowed or applied to the skin. An acute inhalation study has not been submitted. From a study using clothianidin, the active substance of the biocidal product, it is known that no classification is needed for the active ingredient referring to inhalation toxicity. However, there is no specific information about inhalation toxicity of co-formulants (in particular that of the emulsifier) but there is no indication of any hazard caused by the co-formulants via inhalation. More respective information regarding the hazard of the co-formulants should be provided in with the national permission procedure by the notifier. The representative biocidal product is not irritating to the skin or to the eye. Furthermore, there is no evidence for any skin-sensitising potential.

Risk assessment for professionals in this dossier only refers to the active substance clothianidin and its content in the pilot product. By-products have not been considered. Evaluation concentrates on the tasks the participant applied for. A tier 1 approach, which did not take account of safety measures, was sufficient for occupational risk assessment. There was no need to go into further detail because the estimated risks seemed acceptable at all potential exposure scenarios evaluated.

The participant envisaged the use classes 1 to 4 for the clothianidin containing wood preservative product. Evaluation of the submitted information resulted in the necessity to ask for additional data according to Article 10 (1) of Commission Regulation (EC) 2032/2003 in conjunction with Article 11(2) of Directive 98/8/EC to support the use class 4. As a consequence, the participant deleted the use class 4 from the label claim. Assessment of the clothianidin containing wood preservative for application in use classes 1 and 2 was found to be safe. The environmental risk assessment indicates that all scenarios investigated for use class 3 with a wood preservative containing up to 0.05 % clothianidin result in unacceptable risk to the terrestrial environment. Hence, appropriate risk mitigation measures to protect the soil compartment are required at the product authorization stage.

For storage of pre-treated timber after dipping and vacuum pressure treatment the estimated PEC/PNEC ratios pose a risk to the terrestrial compartment including ground-water. In case of a 50 % run-off from the storage place of pre-treated timber after dipping (standard scenario) the PEC/PNEC ratios pose a risk to surface water. Therefore appropriate risk mitigation measures must be applied.

The participant stated that the field of use envisaged should be the application as wood preservative only by professionals and industrial worker.

The representative biocidal product should be used as wood preservative only by professional application in the remedial treatment (use class 1-2, indoor) and in the preventive treatment (use class 1-3).

Evaluation of active substance clothianidin showed the following results: The physico-chemical properties of clothianidin are deemed acceptable for the appropriate use, storage and transportation of the active substance. The evaluation of the active substance has indicated that clothianidin has no carcinogenic and mutagenic potential, no reproductive disturbing properties and is not sensitising (see chapter 2.2.1.1). Clothianidin has shown to be not readily biodegradable. Taking into account the measured log P_{ow} of 0.7 (i.e. log Pow < 3.0) there is no indication of a potential to bioaccumulate. The estimated BCF_{Fish} for the aquatic environment is low (0.78) and confirms this conclusion.

Due to the properties of the active substance clothianidin, an inclusion into Annex IA of the Directive may be possible. However, it has not yet been shown that it is possible to formulate biocidal products containing clothianidin that satisfy the requirements laid down in Article 2 (1) b) of Directive 98/8/EC, i.e. to formulate biocidal products that – under the conditions of use – pose only a low risk to humans, animals, and the environment. Therefore, due to the lack of relevant data, an inclusion of the active substance clothianidin into Annex IA of Directive can currently not be supported.

Overall, it may be expected, that the use of clothianidin in wood preservatives will fulfil the conditions laid down in Article 10 (1) of Directive 98/8/EC and therefore the inclusion into Annex I of Directive 98/8/EC can be recommended.

3.2. Decision regarding Inclusion on Annex I

The substance clothianidin shall be included in Annex I to Directive 98/8/EC as an active substance for use in product-type 8 (wood preservative), subject to the following specific provisions:

The active substance clothianidin, as manufactured, shall have a minimum purity of 950 g/kg.

Member States shall, when performing the assessment in accordance with Article 5 and Annex VI, pay particular attention to the risks to the compartments and populations that have not been addressed in the Community level risk assessment and, when granting product authorisations, ensure that appropriate measures are taken or specific conditions imposed in order to mitigate the identified risks.

Member States shall ensure that authorisations are subject to the following conditions:

In view of the risk identified for the soil, surface water and groundwater compartments, appropriate risk mitigation measures must be taken to protect these compartments. In particular, labels and/or safety-data sheets of products authorised for industrial use indicate that freshly treated timber must be stored after treatment on impermeable hard standing to prevent direct losses to soil and that any losses must be connected for reuse or disposal.

3.3. Factors to be taken into account by Member States when authorising products

The product, which was submitted for Annex I inclusion of clothianidin is a "pilot product", i.e. the product does not really exist and is not placed on the market yet.

The human health risk assessment has been carried out only for professional uses in accordance with the foreseen application of clothianidin containing products. However, when member states are authorizing products, it may be possible to allow appliance of real products for non-professional user, if the outcome of the corresponding risk assessment for non-professionals will support this kind of use.

The environmental risk assessment indicates that application in use classes 1 and 2 was found to be safe. All scenarios investigated for use class 3 with a wood preservative containing up to 0.05 % clothianidin result in unacceptable risk to the terrestrial environment. Therefore, use class 3 may not be permitted for the representative product considered in this evaluation. However, it may be possible to allow appliance of other (real) products in use class 3. If the PEC/PNEC ratios for soil remain greater than 1 for real products (50 cm vertical and horizontal distance) appropriate risk mitigation measures to protect the soil compartment are required at the product authorization stage.

Direct emissions of clothianidin to water bodies from wood in service (use class 3 – e.g. bridge over pond scenario) and in situ application (brushing outdoors) have not been examined. These exposure scenarios and application methods have to be considered in the risk assessment at the stage of product authorisation.

Some information for this pilot product were not submitted by the participant within the procedure of inclusion of an active substance in Annex I of Directive 98/8/EC. For the decision of inclusion of clothianidin in Annex I, these information are dispensable, but for product authorization mandatory. In detail the following data/information have to be submitted for product authorisation:

1. Data to support the efficacy of biocidal products have to be provided for the formulation that is intended to be marketed. In the frame of product evaluation, additional data have to be provided to support the complete requested label claim of the product, i.e. preparation of test specimens has to represent all treatment procedures that are proposed for the application of the products.

2. Submission of analytical methods of any adjuvant in the (real) product with toxicological/ecotoxicological potential.

3. Information according to Art. 20 (3) of the directive for the representative biocidal product is mandatory but not provided by the participant. The necessary elements of labelling have to be provided for the authorisation process of biocidal products containing clothianidin as an active substance.

4. The packaging material of the biocidal product shall be indicated. An expert statement or measured data about possible concentration decrease of the formulation at room temperature have to be provided for the authorisation process of biocidal products containing clothianidin as an active substance.

5. At authorisation stage and depending on the use of the biocidal product, it might be necessary to submit information on the inhalation hazard of co-formulants of the biocidal product

3.4. Requirement for further information

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the inclusion of clothianidin in Annex I to Directive 98/8/EC.

3.5. Recommended Measures

Due to the fact, that for the representative wood preservative different intended uses (spraying, brushing, dipping and vacuum pressure treatment) should be conducted with formulations, which are containing the active substance clothianidin in a range from 0.002 % - 0.1% (w/w %), it seemed necessary to describe measures for a good practice in application.

<u>Occupational Safety Measures</u>

Since inhalation is a common exposure route for professional use of clothianidin it is proposed that member state experts should develop and harmonise an occupational limit value on community level, based on the air concentration of 1.4 mg/m3

Member state experts should develop and harmonise a code of good practice for spray applications since for these processes potential exposure is always high. This code should specify regulations on safety and health at work on community level and give a guidance for authorisation of biocidal products for spray applications.

Environmental protection Measures

As a result of the risk assessment storage of timber treated with clothianidin wood preservative formulations on permeable grounds will pose a risk to soil and groundwater. To remove these concerns during on-site storage of industrial pre-treated timber impermeable grounds (e.g. sealed flooring) are recommended as a condition of use.

In case that the whole leachate run-off from pre-treated timber after dipping and pressure treatment will enter a sewage treatment plant a risk for surface water is indicated. Additionally the leachate run-off related to on site storage of pre-treated timber by dipping will cause a risk to surface water. Therefore, appropriate risk reduction measures should be applied, e.g. all losses must be contained and recycled into the impregnation process or wood is stored under roof. In any case run-offs must be collected and disposed of appropriately.

3.6. Updating this Assessment Report

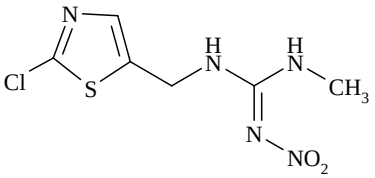
This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information referred to in articles 7, 10.4 and 14 of Directive 98/8/EC. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the inclusion of clothianidin in Annex I to the Directive.

Appendix I: Listing of end points

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

Active substance (ISO Common Name)	Clothianidin
Product-type	Insecticide

Identity

Chemical name (IUPAC)	(E)-1-(2-Chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine
Chemical name (CA)	Guanidine, N-((2-chloro-5-thiazolyl)methyl)-N'-methyl-N"-nitro-, (C(E))-
CAS No	210880-92-5
EC No	433-460-1
Other substance No.	CAS number 131748-59-9 refers generally to TI-435 and its tautomers. This number had been used for TI-435 until the above number was assigned specifically to TI-435.
Minimum purity of the active substance as manufactured (g/kg or g/l)	950 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	No impurities of toxicological, ecotoxicological or environmental concern
Molecular formula	C6H8Cl N5O2S
Molecular mass	249.7 g/mol
Structural formula	

Physical and chemical properties

Melting point (state purity)	176.8°C (purity 99.7%)
Boiling point (state purity)	The test substance decomposed before boiling up to 200 °C.
Temperature of decomposition	decomposition up to 200 °C
Appearance (state purity)	Clear and colourless (Munsell, purity 99.7%) 5Y 8.3/6 (Munsell, purity 97.6%) Solid, powder (purity 99.7% and 97.6%) Odourless (purity 99.7% and 97.6%)
Relative density (state purity)	1.61 at 20°C (purity 99.7%)
Surface tension	79.6 mN/m at 20 °C (90 % saturation)
Vapour pressure (in Pa, state temperature)	1.3 x 10^{-10} Pa (at 25°C) (extrapolated) 3.8 x 10^{-11} Pa (at 20°C) (extrapolated)
Henry's law constant (Pa m^3 mol^{-1})	2.9 x 10^{-11} Pa x m^3 mol -1 (at 20°C)
Solubility in water (g/l or mg/l, state temperature)	pH_4__: 0.304 g/l (at 20 °C) pH_10_: 0.340 g/l (at 20 °C) pH_10_: 0.327 g/l in Milli-Q water (at 20 °C)
Solubility in organic solvents (in g/l or mg/l, state temperature)	Heptane: <0.00104 g/l (at 25°C) Xylene: 0.0128 g/l (at 25°C) Dichloromethane: 1.32 g/l (at 25°C) Methanol: 6.26 g/l (at 25°C) Octanol: 0.938 g/l (at 25°C) Acetone: 15.2 g/l (at 25°C) Ethyl acetate: 2.03 g/l (at 25°C)
Stability in organic solvents used in biocidal products including relevant breakdown products	The active substance clothianidine is thought to be stable within the formulations envisaged
Partition coefficient (log P_{OW}) (state temperature)	pH__4_: 0.893 in buffer at 25 °C (shake-flask method) pH__7_: 0.905 in buffer at 25 °C (shake-flask method) pH_10_: 0.873 in buffer at 25 °C (shake-flask method) 0.7 at 25°C (HPLC method)
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH 5 and 50°C: hydrolytically stable pH 7 and 50°C: hydrolytically stable pH 9 and 50°C: DT_{50} = 14.4 d pH 9 and 20°C: DT_{50} = 1401 d

	(according to Arrhenius equation)
Metabolites at pH 9	CTNU, TZMU, ACT•HCL (formed only at elevated temperatures)
Dissociation constant	pK_a = 11.09 (at 20°C)
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Max. 265.5 nm in acidic and neutral solution, Max. 246.0 nm in basic solution
Photostability (DT_{50}) (aqueous, sunlight, state pH)	pH 7: 3.3 h at 25°C; pH 7,; artificial light with UV filter (λ = 290 nm);
Quantum yield of direct phototransformation in water at Σ > 290 nm	0.014
Oxidizing properties	No oxidising properties
Reactivity towards container material	Following container materials are propose: Polyethylene and austenitic high-grade steel. However, there is no limitation to polyethylene or austenitic high grade steel materials but further examples of proved or advised light tight packaging materials for the solid and the aqueous solution were not given by the participant.
Flammability	Not highly flammable
Explosive properties	Not explosive (when heated and not sensitive to shock and friction)

Classification and proposed labelling

with regard to physical/chemical data	No classification
with regard to toxicological data	Xn; R 22 (Harmful if swallowed)
with regard to fate and behaviour data	N; R 50 (Very toxic to aquatic organisms)
with regard to ecotoxicological data	R°53 (May cause long-term adverse effects in the aquatic environment)

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	HPLC using reversed phase conditions (UV, 265 nm)
Impurities in technical active substance (principle of method)	HPLC

Analytical methods for residues

Soil (principle of method and LOQ)	Parent and metabolites MNG and TZNG LC-MS/MS (ODS or Phenyl-hexyl column) LOQ = 0.005 mg/kg
Air (principle of method and LOQ)	Parent HPLC-UV (RP-18 or CN column) LOQ = 8 µg/m³
Water (principle of method and LOQ)	Parent HPLC-UV (RP-18 or CN column) LOQ = 0.05 µg/L (drinking and surface water)
Body fluids and tissues (principle of method and LOQ)	Not required
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not required
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Rapid oral absorption, bioavailability >90 %
Rate and extent of dermal absorption:	2 %, based on an *in vivo* study in rhesus monkeys
Distribution:	Widely distributed; tissue residues (72 hours): 0.3 %, mainly liver and kidney
Potential for accumulation:	No potential for accumulation
Rate and extent of excretion:	Rapid, within 24h: urine: 89-95 % (low dose), 57 % (high dose), faeces: 3-8 %, air: 0.017 %; limited enterohepatic circulation
Toxicologically significant metabolite(s)	Parent compound 56-74%, TZNG and MNG ≥10%, MTCA ~8.5%, NTG ≤ 4% of applied dose + 9 further metabolites < 2%

Acute toxicity

Rat LD_{50} oral	Males: 1216 < LD_{50} < 2000 mg/kg bw Females: 523 < LD_{50} < 1216 mg/kg bw
Mouse LD_{50} oral	Males: 389 mg/kg bw Females: 465 mg/kg bw
Rat LD_{50} dermal	> 2000 mg/kg bw
Rat LC_{50} inhalation	> 6.141 mg/L air (4 h exposure, head only)
Skin irritation	Not irritant
Eye irritation	Not irritant
Skin sensitization (test method used and result)	Not sensitising (M & K)

Short-term repeated dose toxicity

Species/ target / critical effect	Haematopoetic organs (rat, dog); kidney (mouse)
Oral NOAEL / LOAEL	NO(A)EL: 650 ppm; 20 mg/kg bw/day (90 d dog: WBC decrease; NOEL: 100 ppm; 16 mg/kg bw/day (M) (90 d mouse: mortality)
Dermal NOAEL / LOAEL	NOAEL >1000 mg/kg bw (M+F) (28 d rat)
Inhalation NOAEL / LOAEL	No data, no study required

Genotoxicity	No genotoxic potential

Chronic Toxicity/Carcinogenicity

Species/ target / critical effect	Interstitial ovarial gland hyperplasia, bw effects, feed consumption (2 yr rat)
Relevant dermal NOAEL / NOEL	9.7 mg/kg bw/d

Carcinogenicity	No carcinogenic potential

Reproductive toxicity

Reproduction toxicity

Species/ Reproduction target / critical effect	Rat: slight effects on sperm motility and morphology; increased stillborn pup incidence; decreased perinatal viability, decreased birth weight and postnatal body weight gain, delayed male sexual maturation
Parental NOAEL / LOAEL	NOAEL parental: 31/37 mg/kg bw/d, (M/F)
Reproductive NOAEL / LOAEL	NOAEL reproduction: 31 mg/kg bw/d
Offspring NOAEL / LOAEL	NOAEL offspring: 10 mg/kg bw/d

Developmental toxicity

Developmental target/critical effect	Rabbit: abnormalities of lung lobation, embryolethality, decreased foetal weight, decreased ossification Rat: delayed postnatal growth and development delayed
Relevant maternal NOAEL	NOAEL maternal: 25 mg/kg bw/d (rabbit)
Relevant developmental NOAEL	NOAEL foetal: 25 mg/kg bw/d (rabbit)

Neurotoxicity

Acute neurotoxicity	Rat: Acute neurotoxicity NOAEL: 60 mg/kg bw/d (*tremors, locomotor activity, hypothermia*)
Repeated neurotoxicity	Rat: Short-term neurotoxicity NOAEL: 177 mg/kg bw/d
Delayed neurotoxicity	Rat: Developmental neurotoxicity NOAEL: 43 mg/kg bw/d (startle habituation, motor activity)

Other studies

Metabolite data

Acute toxicity	TZNG: LD_{50} (M/F) >1450/1481 mg/kg bw TMG: LD_{50} (M/F) <550/567 mg/kg bw TZMU: LD_{50} (M/F) 1424/1282 mg/kg bw MG: LD_{50} (M/F) 550/446 mg/kg bw

Genotoxicity	MNG, TZNG, TMG, TZMU, MG: no genotoxic potential
Investigation on enzyme induction	Slight enzymatic induction potential in the liver; no influence on thyroid hormone activity (T_3, T_4, TSH) in 90d rat study Effects consistent with nicotinic CNS-stimulation and depression
Pharmacological studies	Mouse: decreased activity, increased hexobarbital-induced sleeping time, convulsions following sub-threshold electroshock, decreased intestinal transport, decreased hindlimb support NOAEL : 25 mg/kg

Medical data

.....	No data: new compound

Summary	Value	Study	Safety factor OA*
Non-professional user			
AEL_{acute}*	0.25 mg/kg bw	Pharmacology study, mouse	100
$AEL_{medium-term}$*	0.2 mg/kg bw/d	90-d dog, supported by 90-d rat and embryotoxicity rabbit	100 / > 90 %**
$AEL_{long-term}$*	0.1 mg/kg bw/d	2-yr rat, supported by 2-gen. rat	100
ADI (if residues in food or feed)***	-	-	-
ARfD (if residues in food or feed)***	-	-	-
Professional user			
Reference value for inhalation (proposed OEL)	1.4 mg/m^3	chronic results (2-yr rat)	25
Reference value for dermal exposure	not specified	for Tier 1 risk assessment the ADI is used	n.a.

* AEL: Systemic (= Internal) Acceptable Exposure Level

** Oral absoption

*** Not relevant for Annex I inclusion of clothianidin PT 8

Acceptable exposure scenarios (including method of calculation)

Professional users

Production of active substance:	No evaluation; clothianidin is produced outside the EU in Japan	
Formulation of biocidal product	Weighing of solid a.s / filling of 0.1% active substance	
Weighing and controlling of the dosage procedure (LEV present), Form of exposure: dust active substance Duration: 15 min. Frequency: daily no PPE	Potential inhalation exposure (weighing)	0.2 mg/m^3
	Potential dermal exposure (weighing, filling)	85 mg/person/day
Filling of the liquid biocidal product (0.1 % active substance) into 1000 l containers Duration: 150 min., Frequency: daily Form of exposure: liquid (0.1% active substance) Model: EASE 2.0		
Intended use: spraying	Conc. biocidal product 0.1 % active substance	
Mixing & loading: loading sprayer, priming pump and spray line	Potential inhalation exposure (application)	0.03 mg/m^3
Application: spray pressure: 4-7 bar, indoor use, direction: overhead, Form of exposure: aerosol during spraying Duration spraying: 80 min., Frequency: 3 days a week Model: TNsG Human Exposure Model 2 Spraying Post-application: Unblock spray nozzle, cleaning Model post-application: RISKOFDERM DEO unit	Potential dermal exposure (all phases)	203.5 mg/person/day
Intended use: brushing	Conc. biocidal product 0.1 %	
Application method: brushing, direction: level, Duration: 8 h, Frequency: 3 days a week no PPE	Potential inhalation exposure (all phases)	negligible (expert judgement)
Model for all phases: maximum deposition 12 mg/cm^2 skin, exposed skin : forearms, hands (back + palm), thighs	Potential dermal exposure (all phases)	47 mg/person/day
Intended use: vacuum pressure process	Conc. biocidal product 0.05 %, the biocidal product is diluted for application to an aqueous solution containing 0.002 % of the active substance	
Mixing & loading: connecting lines Form of exposure: liquid (0.05 % active substance) Frequency: once a week	Potential inhalation exposure (application)	2.9 x 10^{-5} mg/m^3

Model: Maximum deposition 12 mg/cm^2 skin Application: loading and unloading treated wood, opening of vessel Form of exposure: liquid/aerosol (0.002 % active substance) Duration: 6 hours, 2 cycles per day Frequency daily Model: TNsG Human Exposure Model 1 Handling Post-application: cleaning and maintenance work Form of exposure: liquid (0.002 % active substance) Duration: 30 min. Frequency: once a week Model: TNsG Human Exposure Model 1 Handling	Potential dermal exposure (all phases)	6.0 mg/person/day
Intended use: dipping / immersion	Conc. biocidal product 0.05 %, the biocidal product is diluted for application to an aqueous solution containing 0.0075 % of the active substance	
Mixing & loading: connecting lines Form of exposure: liquid (0.05 % active substance) Frequency: once a week Model: Maximum deposition 12 mg/cm^2 skin Application: loading and unloading treated wood Form of exposure: liquid (0.0075 % active substance) Duration: 5 cycles per day Frequency daily Model: TNsG Human Exposure Model 1 Handling Post-application: cleaning and maintenance work Form of exposure: liquid (0.0075 % active substance) Duration: 30 min. Frequency: once a week Model: TNsG Human Exposure Model 1 Handling	Potential inhalation exposure (all phases)	negligible(expert judgement)
	Potential dermal exposure (all phases)	10.7 mg/person/day
Secondary exposure	Mechanical processing of treated wood (sawing, sanding, wiping)	
Sawing/sanding of treated wood Form of exposure: dust of treated wood Duration: shift Frequency: daily Model: expert judgement on the basis of maximum exposure of 5 mg/m^3 to wood dust	Potential inhalation exposure	0.0004 mg/m^3
Wiping residues Form of exposure: residues of active substance Model: maximum deposition 12 mg/cm^2 skin	Potential dermal exposure	0.16 mg/person/day
Non-professional users	Not applicable	
Indirect exposure as a result of use	Uses acceptable, no residues via food and feed expected	

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 and 50°C: hydrolytically stable
	pH 7 and 50°C: hydrolytically stable
	pH 9 and 50°C: DT_{50} = 14.4 d pH 9 and 20°C: DT_{50} = 1401 d (according to Arrhenius equation)
Metabolites at pH 9	CTNU, TZMU, ACT•HCL (formed only at elevated temperatures)
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	DT_{50} = 3.3 h (experimental value), pH 7, artificial light with UV filter (λ = 290 nm) Major degradation products (> 10 % of the applied radioactivity): TZMU, MG, HMIO, FA, MU, CO_2. Modelled DT_{50} for the 50th degree of latitude: up to 23.4 d
Quantum yield of direct photolysis at T > 290 nm	0.014
Readily biodegradable (yes/no)	No
Biodegradation in seawater	Not relevant for intended use
Non-extractable residues (bound residues)	Aerobic: 27.6 – 43.3 % after 100 d Anaerobic: 80.9 % after 360d
Distribution in water / sediment systems (active substance)	Aerobic at 20°C in the dark, 100 d: Water: max. 92.3 % (day 0); decline to 8.8 % (day 100) Sediment: max. 37.3 % (day 7) DT_{50} (dissipation) = 30.8 and 49.8 d (water) DT_{50} = 48.0 and 64.8 d (entire system) Converted to average EU outdoor temperature of 12°C: DT_{50} (dissipation, 12°C) = 58 and 94 d (water) DT_{50} (12°C) = 91 and 123 d (entire system) Mineralisation: < 4.5 % after 100d Anaerobic at 20°C in the dark, 360 d: Water: max. 87.4 % (day 0); decline to 1 % (day 90) Sediment: max. 41.2 % (day 3) DT_{50} (dissipation) = 4 d (water) DT_{50} = 21 d (entire system) Converted to average EU outdoor temperature of 12°C: DT_{50} (dissipation, 12°C) = 7.6 d (water) DT_{50} (12°C) = 40 d (entire system)

	Mineralisation < 0.1 %
Distribution in water / sediment systems (metabolites)	Aerobic: Water: no metabolite detected Sediment: TMG at max. level of 22.9 % (day 58) Anaerobic: Water: no metabolite detected Sediment: no metabolite > 5 %

Route and rate of degradation in soil

Mineralization (aerobic)	max. 8.8% after 90 d max. 11.2% after 120d max. 14.8 % after 365 d
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20°C, aerobic): 143 d – > 1 year (9 soils, median= 541 d, R^2 = 0.72 – 0.99) DT_{50lab} (converted to 12°C, aerobic): 271 d – > 1 year
	DT_{90lab} (20°C, aerobic): ---
	DT_{50lab} (10°C, aerobic): ---
	DT_{50lab} (20°C, anaerobic): ---
	degradation in the saturated zone: no data
Field studies (state location, range or median with number of measurements)	Clothianidin: $DT_{50field}$ (20°C, geometric mean, recalculated) = 274 d $DT_{50field}$ (12°C, geometric mean, recalculated) = 515 d After 24 months 19 % (bare soils), 8 % and 31 % (cropped soils) of the applied amount based on the active substance were recovered from the soil
	DT_{90f}:
Anaerobic degradation	No data
Soil photolysis	No data
Non-extractable residues	max. 7.5 % after 90 d max. 9.4 % after 120 d max. 12.8 % after 365 d
Relevant metabolites - name and/or code, % of applied active substances (range and maximum)	MNG: Aerobic at 20°C in the dark, 120 d Max. 10.7 % after 120d (4 soils) DT_{50} = 82 – 108 d (3 soils) DT_{50} (converted to 12°C): 156 – 205 d Mineralization: max. 13 % after 90 d, max. 17 % after 120 d

	Bound residues: max. 14 % after 90 d, max. 16 % after 120d TZNG: Aerobic at 20°C in the dark, 120 d Max. 9.1 % after 120 d (4 soils) DT_{50} = 62 – 111 d (3 soils) DT_{50} (converted to 12°C): 118 – 211 d Mineralization: max. 15 % after 90 d; max. 19 % after 120 d Bound residues: max. 14 % after 90 d, max. 16 % after 120
Soil accumulation and plateau concentration	No data

Adsorption/desorption

Ka , Kd, Ka/Kd	Ka (n=5): 0.52 – 4.14 ml g^{-1} (geometric mean: 1.3 ml g^{-1}), 1/n: 0.81 – 0.87; Kd (n=5): 0.62 – 4.58 ml g^{-1} (geometric mean: 1.5 ml g^{-1}), 1/n: 0.81 – 0.88; Ka/Kd (n=5): 0.69 – 0.90; mobility: medium to high
Ka_{oc} , Kd_{oc}	Ka_{OC} (n=5): 84 – 345 ml g^{-1} (geometric mean: 140 ml g^{-1}); Kd_{OC} (n=5): 95 – 382 ml g^{-1} (geometric mean: 168 ml g^{-1})
pH dependence (yes / no) (if yes type of dependence)	No
Metabolites: MNG: Ka, Kd, Ka/Kd	Ka (n=5): 0.02 – 0.37 ml g^{-1} (geometric mean: 0.11 ml g^{-1}), 1/n: 0.70 – 1.10; Kd (n=3): 0.15 – 0.48 ml g^{-1} (geometric mean: 0.30 ml g^{-1}), 1/n: 0.88 – 0.97; Ka/Kd (n=3): 0.72 – 1.27; mobility: very high
Ka_{oc}, Kd_{oc}	Ka_{OC} (n=5): 5.2 – 34.3 ml g^{-1} (geometric mean: 17 ml g^{-1}); Kd_{OC} (n=3): 13.0 – 44.0 ml g^{-1} (geometric mean: 27 ml g^{-1})
TZNG: Ka, Kd, Ka/Kd	Ka (n=5): 0.63 – 4.71 ml g^{-1} (geometric mean: 1.7 ml g^{-1}), 1/n: 0.78 – 0.90; Kd (n=5): 0.83 – 5.75 ml g^{-1} (geometric mean: 2.1 ml g^{-1}), 1/n: 0.79 – 0.90; Ka/Kd (n=5): 0.76 – 0.88;

	mobility: moderate
Ka_{oc}, Kd_{oc}	Ka_{OC} (n=5): 205 – 433 ml g^{-1} (geometric mean: 266 ml g^{-1}); Kd_{OC} (n=5): 271 – 527 ml g^{-1} (geometric mean: 329 ml g^{-1})

Mobility in soil

Mobility in soil	3 lysimeters: undisturbed soil, 1 m^2 surface, 1.3 m depth, sandy loam, 1.8 % organic C, pH 6.6 Lysimeter 1: cereals, application of active substance 100 g in year 1 and 138 g in year 2, annual rainfall: 878 – 912 mm Lysimeter 2 and 3: grass, application of active substance 160 g in yer 1 and 2, annual rainfall: 847 – 930 mm Leachates: active substance: not found, MNG: max. 0.066 µg L^{-1}, TZNG: not found, NTG: max. 0.031 µg L^{-1}, U3 (unknown metabolite): 0.072 µg L^{-1}

Fate and behaviour in air

Direct photolysis in air	No data
Quantum yield of direct photolysis at T >290 nm	No data
Photo-oxidative degradation in air	Estimation method (AOPWIN) with 24-hours-mean-day concentration of $5x10^5$ OH radical cm^{-3} Half-life: 2.8 h Chemical lifetime: 4.1 h
Volatilization	Not relevant (refer to chapter 1, Henry's law constant)

Monitoring data, if available

Soil (indicate location and type of study)	No data
Surface water (indicate location and type of study)	No data
Ground water (indicate location and type of study)	No data
Air (indicate location and type of study)	No data

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	96 h	mortality	LC_{50} > 100 mg/l
Pimephales promelas	33 d	hatching, mortality and growth	NOEC ≥ 20 mg/l

Invertebrates			
Daphnia magna	48 h	immobility	EC_{50} = 26‡ mg/l
Daphnia magna	21 d	mortality, reproduction	NOEC = 0.12 mg/l
Chironomus riparius	48 h	mortality	EC_{50} = 0.029 mg/l
Chironomus riparius	28 d	emergence, development	EC10 = 0.00065 mg/l
Algae			
Selenastrum capricornutum	96 h	growth inhibition	E_bC_{50} = 56 mg/l NOEC = 15 mg/l
Microorganisms			
Activated sludge from sewage treatment plant	3 h stat.	respiration inhibition	EC_{50} > 1000 mg/L
Freshwater species community			
Sediment dwelling organisms, phytoplankton and zooplankton	14 weeks	mesocosm	NOEC = 1 µg/l

Effects on earthworms or other soil non-target organisms

Acute toxicity to *earthworms*	*Eisenia foetida* LC_{50} (14 d) = 13.21 mg/kg dwt soil (mortality)
Long-term toxicity to earthworms	*Eisenia foetida* NOEC (56 d) = 0.1 mg/kg dwt soil* (mortality, reproduction)
Long-term toxicity to other soil non-target macro-organisms	*Folsomia candida* NOEC (28 d) = 0.32 mg/kg dwt soil (mortality, reproduction)

*assuming a soil depth of 10 cm and a soil density of 1500 kg/m³ for dry soil

‡ *in the evaluation of the same test under PPPD 91/414/EC an EC_{50} of 40 mg/L was derived. However 70 % effect was reported at 32 mg/L test concentration. Therefore a recalculation of the EC_{50} value was performed resulting in an EC_{50} of 26 mg/L.*

Effects on soil micro-organisms

Nitrogen mineralization	< 25% effects at 0.1 mg and 0,5 mg active substance* NOEC = 0.5 mg/kg dwt soil
Carbon mineralization	< 25% effects at 0.1 mg and 0,5 mg active substance* NOEC = 0.5 mg/kg dwt soil

*assuming a soil depth of 10 cm and a soil density of 1500 kg/m³ for dry soil

Effect on terrestrial plants

Acute toxicity to plants (10 species)	NOEC (15 d) ≥ 0.15 mg/kg dwt soil* (emergence, growth)
Acute toxicity to plants (10 species)	NOEC (15 d) ≥ 0.15 mg/kg dwt soil* (growth, phytotoxicity)

*assuming a soil depth of 10 cm and a soil density of 1500 kg/m³ for dry soil

Effects on terrestrial vertebrates

Acute toxicity to mammals	See LOEP chapter 3 “Acute toxicity”
Acute toxicity to birds	*Coturnix japonica* $LC(D)_{50}$ = 430 mg/kg bw
Dietary toxicity to birds	*Anas platyrhynchos* $LC(D)_{50}$ (5 d) > 5200 mg/kg food
Reproductive toxicity to birds	*Colinus virginianus*, *Anas platyrhynchos* NOEC (147 d) ≥ 500 mg/kg food

Effects on honeybees

Acute oral toxicity	No data
Acute contact toxicity	No data

Effects on other beneficial arthropods

Acute oral toxicity	No data
Acute contact toxicity	No data
Acute toxicity to ……..	No data

Bioconcentration

Bioconcentration factor (BCF)	BCF_{fish} = 0.78 (calc.) $BCF_{earthworm}$ = 0.9 (calc.)
Depration time (DT_{50}) (DT_{90})	n.d.

Level of metabolites (%) in organisms accounting for > 10 % of residues	n.d.

Chapter 6: Other End Points

No

Appendix II: List of Intended Uses

The intended uses of the representative wood preservative are only for professional application. For remedial treatment of indoor wood (use class 1 and use class 2) the biocidal product is intended to be used only as a ready-for-use product. Water-based formulations containing 0.05 % clothianidin are proposed for dipping treatments and vacuum pressure treatment.

The submitted studies indicate preventive action of clothianidin against termites and beetles. The tests have been performed with the active substance clothianidin in ethanol. Tests that have been performed with a pilot product indicate a limited curative action of this product.

Summary of intended uses

Product type	Field of use envisaged		Likely concentration at which active substance will be used (w/w %)	Applied amount per treatment (mg as/m^2 wood)	Effective retention in wood
PT 8	**professional use only**	Remedial treatment (insect control in wood in use): spraying , use class 1-2	0.1 %	250	250 mg as/m² wood
		Remedial treatment (insect control in wood in use) brushing, use class 1-2	0.1 %	250	250 mg as/m² wood
		Protective insect control dipping, use class 1-3	0.05 %	15-20	15 mg as/m^2 wood 30-40 g of 0.05% product correspond to 15-20 mg as/m²
		Protective insect control vacuum pressure treatment, use class 1-3	0.05 %	250	10 g as/m^3 wood 20 kg/m³ of 0.05% product correspomd to 10 g as/m³**

**Conversion from g as/m³ wood to g as/m² wood is based on the assumption that 1 m³ of wood corresponds to 40 m² wood (which is the case for over 90 % of treated construction timber).

Appendix III: List of Studies

The references/studies listed below are those included in the German Competent authority report for clothianidin in wood preservatives (PT 8).

Data protection is claimed by Sumitomo Chemical Takeda Agro Company, Ltd., United Kingdom, in accordance with Article 12.1(c) (i) and (ii) of Council Directive 98/8/EC for all study reports marked "yes" in the "Data Protection Claimed" column of the table below. For studies marked "yes" data protection is claimed under Article 12.1(c)(ii). Since there has not been a national legislation on biocides in Germany no studies have been seen before by the RMS. Therefore, these claims are based entirely on information from the applicant. It is assumed that the relevant studies are not already protected in any other Member State of the European Union under existing national rules relating to biocidal products. It is not possible for the Rapporteur Member State to confirm the accuracy of this information.

The data which has been marked with * in the tables are from studies where a full STUDY SUMMARY according to TNsG for Dossier Preparation and Study Evaluation is available, i.e. the KEY STUDIES.

Section No./ reference No.	Author(s)	Year	Title	Data Protec. claimed (yes/no)	Owner
Doc II A4, Doc II B7, Doc II B10		1999	Directive 1999/45/EC of the European Parliament and of the Council concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations.	No	Public
Doc II A5	Schmuck,R. & Keppler, J.	2003	Clothianidin – Ecotoxicological profile and risk assessment. Pflanzenschutz-nachrichten Bayer 56 (1), 26-58.	No	Published
Doc II B8	Nauen, R., *et al*.	2001	Acetylcholine receptors as sites for developing neonicotinoid insecticides: Biochemical Sites of Insecticide Action and Resistance (Ed. I. Ishaaya), Springer-Verlag Berlin, Heidelberg, pp. 77-105Date: 2001non-GLP, published	No	Published
Doc II B10		1991	Council Directive 91/414/EEC concerning the placing of plant protection products on the market	No	Public
Doc II B9	EU	2004	Human Exposure to Biocidal Products (TNsG June 2002), User Guidance Document	No	Published
Doc II B9	SAIC, Science Applications International Corporation	1996	Occupational dermal exposure assessment, A review of methodologies and field data	No	Published
Doc II B9	EU	June 2002a	Technical Notes for Guidance: Human Exposure to Biocidal Products - Guidance on Exposure Estimation [„Report 2002“ http://ecb.jrc.it/biocides]	No	Published
Doc II B9	US EPA	1995	Exposure Factors Handbook	No	Published
Doc II B9	R. Guiver, H. Chambers, R. Foster, P. Johnson, D. Rimmer	1999	A report of 16 visits addressing occupational exposure arising from dipping activities with biocides and non agricultural pesticides. 3830/R51.169	No	Published

Doc II B9 Doc II C13		2002	European Chemicals Bureau (ECB 2002): Technical Notes for Guidance in Support of Directive 98/8/EC of the European Parliament and the Council Concerning the Placing of Biocidal Products on the Market. Human Exposure to Biocidal Products, Guidance on Exposure Estimation, Part 3, Final draft.	No	Public
Doc II B9	BAM	2005	Inter-laboratory Evaluation of Laboratory Test Methods to estimate the Leaching from Treated Wood. EC Grant Agreement No. 04/375757/C4, April 2005).	No	Published
Doc II B9	OECD	2003	OECD SERIES ON EMISSION SCENARIO DOCUMENTS, Number 2. Emission Scenario Document for Wood Preservitives, Part 1.	No	Published
Doc II C13	European Chemicals Bureau	2002b	Technical Notes for Guidance in Support of Directive 98/8/EC of the European Parliament and the Council Concerning the Placing of Biocidal Products on the Market. Human Exposure to Biocidal Products, Guidance on Exposure Estimation. Final draft	No	Published
Doc II C13	European Chemicals Bureau	2005	Technical Guidance Documents in Support of Directive 93/87/EEC on Risk Assessment for New Notified Substances and The Commission Regulation (EC) 1488/94 on Risk Assessment for Existing Substances, Part I, Chapter 4, Human Risk Characterisation, Revision Document TGD_H_RC_dr_ECB_01.doc	No	Published
Doc II C13		2001	International Programme on Chemical Safety (IPCS) of the World Health Organisation (2001): Guidance Document for the Use of Data in Development of Chemical-Specific Adjustment Factors (CSAFs) for Interspecies Differences and Human Variability in Dose/Concentration–Response Assessment.	No	Public
Doc II C13	Renwick, AG	1993	Renwick, AG (1993): Data-derived safety factors for the evaluation of food additives and environmental contaminants. Food Addit Contam (10), 275–305, 1993	No	Public
Doc II C14	BAM	2005	Expert judgement, personal communication		
Doc II C16	AGS	2003	German Technical Rule for Hazardous Substances (TRGS) 523 “Pest Control with Very Toxic, Toxic and Harmful Substances and Preparations	No	Published
Doc II C16	European Chemicals Bureau	2003	Technical Guidance Documents in Support of Directive 93/87/EEC on Risk Assessment for New Notified Substances and The Commission Regulation (EC) 1488/94 on Risk Assessment for Existing Substances, Part I, Chapter 2, Effects Assessment, EUR 20418 EN/1	No	Published
Doc II C16	EU	1988	EU Directive 88/379/EEC Council Directive of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances	No	Published
Doc II C16	DE	2004	Verordnung zum Schutz vor Gefahrstoffen (Gefahrstoffverordnung – GefStoffV)	No	Published

Doc II C16	DE	1999	Allgemeine Verwaltungsvorschrift zum Wasserhaushaltsgesetz über die Einstufung wassergefährdender Stoffe in Wassergefährdungsklassen (Verwaltungsvorschrift wassergefährdende Stoffe – VwVwS)	No	Published
Doc II C16	EU	2001	European Waste Catalogue Commission Decision 2000/532/EC of 16 January 2001 as regards the list of wastes	No	Published
Doc III A					
A 1.3.2.1*	Morrissey, M. A. & Kramer, H. T.	2000 b	Vapor pressure of TI-435, pure active ingredient, Covance, report no.6155-115A, April 10, 2000, unpublished, Sumitomo Chemical Takeda Agro Co., Ltd.	yes	Sumi Take
A3.1.1/01	Kamiya, Y.	2000a	Determination of melting point/melting range of TI-435 pure active ingredient (PAI). Takeda Chemical Industries, Japan, report no. PC'00-09 SumiTake report no. DPCI008 April 12, 2000 GLP, unpublished	yes	SumiTake
A3.1.2/01	Kamiya, Y.	2000b	Determination of boiling point of TI-435 pure active ingredient (PAI). Takeda Chemical Industries, Japan, no report number given SumiTake report no. DPCI085 April 19, 2000non-GLP, unpublished	yes	SumiTake
A3.1.3/01*	Morrissey, M.A.; Kramer, H.T.	2000a	Determination of dissociation constant and physical-chemical properties of TI-435 pure active ingredient (PAI) (density, solubility, octanol/water partition coefficient and dissociation constant). Covance, USA, report no. 6155-122 SumiTake report no. DPCI015 April 10, 2000 Amendment no. 3 of July 26, 2001 GLP, unpublished	yes	SumiTake
A3.1.3/02	Kramer, H.T.; Telleen, K.	2000	Physical-chemistry tests with TI-435 technical grade active ingredient (TGAI). Covance, USA, report no. 6155-117 SumiTake report no. DPCI018 December 21, 2000 GLP, unpublished	yes	SumiTake
A3.10/01	Kramer, H.T.; Telleen, K.	2000	see A3.1.3/02		
A3.11/01	Wright, E.	2000	TI-435 (technical grade active ingredient): Evaluation of the flammability (EC test A 10). Covance Ltd., report no. 586/235-D2141 SumiTake report no. DPCI001 March 14, 2000 GLP, unpublished	yes	SumiTake
A3.11/02	Kramer, H.T.; Telleen, K.	2000	see A3.1.3/02		
A3.13/01	Kramer, H.T.; Telleen, K.	2000	see A3.1.3/02		
A3.15/01	Kramer, H.T.; Telleen, K.	2000	see A3.1.3/02		

A3.16/01	Kramer, H.T.; Telleen, K.	2000	see A3.1.3/02		
A3.17/01	Kramer, H.T.; Telleen, K.J.	2002	Storage stability of TI 435 (0, 3, 6, 9, 12, 18, & 24 month time points). Covance, USA, report no. 6155-116 SumiTake report no. DPCI013 June 20, 2002 GLP, unpublished	yes	SumiTake
A3.17/02	Kramer, H.T.; Telleen, K.	2000	see A3.1.3/02		
A3.2.1/01	Morrissey, M.A.; Kramer, H.T.	2000b	see A3.2/01		
A3.2/01	Morrissey, M.A.; Kramer, H.T.	2000b	Vapor pressure of TI-435, pure active ingredient. Covance, USA, report no. 6155-115A SumiTake report no. DPCI014 April 10, 2000 GLP, unpublished	yes	SumiTake
A3.3.1/01	Kamiya, Y.	2000c	Determination of physical state of TI-435 pure active ingredient (PAI).Takeda Chemical Industries, Japan, report no. PC'00-05 SumiTake report no. DPCI006 April 12, 2000 GLP, unpublished	yes	SumiTake
A3.3.1/02	Kamiya, Y.	2000d	Determination of physical state of TI-435 technical grade of the active ingredient (TGAI). Takeda Chemical Industries, Japan, report no. PC'00-48 SumiTake report no. DPCI003 July 13, 2000 GLP, unpublished	yes	SumiTake
A3.3.2/01	Kamiya, Y.	2000e	Determination of color of TI-435 pure active ingredient (PAI).Takeda Chemical Industries, Japan, report no. PC'00-04 SumiTake report no. DPCI005 April 12, 2000 GLP, unpublished	yes	SumiTake
A3.3.2/02	Kamiya, Y.	2000f	Determination of color of TI-435 technical grade of the active ingredient (TGAI).Takeda Chemical Industries, Japan, report no. PC'00-47 SumiTake report no. DPCI002 July 13, 2000 GLP, unpublished	yes	SumiTake
A3.3.3/01	Kamiya, Y.	2000g	Determination of odor of TI-435 pure active ingredient (PAI).Takeda Chemical Industries, Japan, report no. PC'00-06 SumiTake report no. DPCI007 April 12, 2000GLP, unpublished	yes	SumiTake
A3.3.3/02	Kamiya, Y.	2000h	Determination of odor of TI-435 technical grade of the active ingredient (TGAI). Takeda Chemical Industries, Japan, report no. PC'00-49 SumiTake report no. DPCI004 July 13, 2000 GLP, unpublished	yes	SumiTake
A3.4/01	Mikata, K.	2000	Determination of UV/VIS absorption spectrum of TI-435 pure active ingredient (PAI).Takeda Chemical Industries, Japan, report no. PC'00-03 SumiTake report no. DPCI009 April 10, 2000 GLP, unpublished	yes	SumiTake
A3.4/02	Kamiya, Y.	2000i	Determination of infrared (IR) absorption spectrum of TI-435 pure active ingredient (PAI).Takeda Chemical Industries, Japan, report no. PC'00-08 SumiTake report no. DPCI010 April 12, 2000 (Amendment no. 1 of July 11, 2001) GLP, unpublished	yes	SumiTake

A3.4/03	Kamiya, Y.	2000j	Determination of nuclear magnetic resonance (NMR) spectrum of TI-435 pure active ingredient (PAI).Takeda Chemical Industries, Japan, report no. PC'00-07 SumiTake report no. DPCI011 April 12, 2000 GLP, unpublished	yes	SumiTake
A3.4/04	Yanai, T.	2000	Determination of mass spectrum of TI-435 PAI. Takeda Chemical Industries, Japan, report no. PC'00-01 SumiTake report no. DPCI012 January 21, 2000 GLP, unpublished	yes	SumiTake
A3.5/01	Morrissey, M.A.; Kramer, H.T.	2000a	see A3.1.3/01		
A3.5/02	O'Connor, B.J.; Mullee, D.M.	2001	TI-435 (Pure Active Ingredient, PAI): Determination of the effect of pH on water solubility and partition coefficient Safepharm Lab. Ltd., report no. 178/125 SumiTake report no. DPCI068 November 9, 2001 GLP, unpublished	yes	SumiTake
A3.6/01	Morrissey, M.A.; Kramer, H.T.	2000a	see A3.1.3/01		
A3.7/01	Morrissey, M.A.; Kramer, H.T.	2000a	see A3.1.3/01		
A3.9/01	Morrissey, M.A.; Kramer, H.T.	2000a	see A3.1.3/01		
A3.9/02	O'Connor, B.J.; Mullee, D.M.	2001	see A3.5/02		
A4.1/01*	Kramer, H.T. Telleen, K.	2001a	Analytical method for analysis of TI-435 technical grade active ingredient (TGAI). Covance, part of report no. 6155-119 SumiTake report no. DPCI019 March 1, 2001 non-GLP, unpublished	yes	SumiTake
A4.1/02* filed in confidential section	Kramer, H.T. Telleen, K.	2001b	Preliminary analysis of TI-435 technical grade active ingredient (TGAI). Covance revised report no. 6155-119 SumiTake report no. DPCI016 January 10, 2001, amended on January 15, 2002 and January 17, 2003	yes	SumiTake
A4.2*	Schramel, O.	1999	Residue analytical method 00521 (MR-metabolites TZNG, TZMU, MNG and TMG in soil by Liquid Chromatography with electrospray MS/MS-detection. Bayer AG, report no. MR-343/98 SumiTake 343/98) for determination of TI-435 and the report no. DEFT003; P60180012 October 14, 1999 GLP, unpublished	yes	SumiTake / Bayer
A4.2/01*	Schramel, O.	2000a	Residue analytical method 00540 (MR-654/98) for determination of TI-435 and the metabolites TZNG and MNG in soil by Liquid Chromatography with electrospray MS/MS-detection. Bayer AG, report no. MR-654/98 SumiTake report no. DEFT007; P60180010 January 24, 2000	yes	SumiTake / Bayer

			GLP, unpublished		
A4.2/02*	Hellpointner, E.	2000	Method for the determination of TI-435 in air by HPLC-UV and confirmation of the method by HPLC-UV using a CN phase. Bayer AG, report no. HPO-203, report ID MR-370/00 SumiTake report no. DEFT017; P60576005 September 14, 2000 GLP, unpublished	yes	SumiTake / Bayer
A4.2/03*	Weber, H.	2000	Enforcement method 00659 for the determination of the residues of TI-435 in drinking and surface water. DR. SPECHT & PARTNER, report no. BAY-0009V / Az. G00-0065 SumiTake report no. DEFT034 November 30, 2000; 1st addendum March 13, 2001 GLP, unpublished	yes	SumiTake / Bayer
A4.2/04	Weber, H.	2000a	Enforcement method 00658 for the determination of the residues of TI-435 in soil. DR. SPECHT & PARTNER, report no. BAY-0010V / Az. G00-0066 SumiTake report no. DEFT033 November 30, 2000; 1st addendum March 13, 2001 GLP, unpublished	yes	SumiTake / Bayer
A4.3/01	Weber, H.	2000c	Enforcement method 00657 for the determination of the residues of TI-435 in plant material. DR. SPECHT & PARTNER, report no. BAY-0007V / Az. G00-0063 SumiTake report no. DRES013 November 30, 2000; 1st addendum February 16, 2001 GLP, unpublished	yes	SumiTake / Bayer
A4.3/02	Weber, H.	2001	Enforcement method 00657/M001 for the determination of the residues of TI-435 in plant material. DR. SPECHT & PARTNER, report no. BAY-0113V / Az. G01-0098 November 16, 2001 GLP, unpublished	yes	SumiTake / Bayer
A5.4.1/01	Nauen, R., *et al*.	2001	Acetylcholine receptors as sites for developing neonicotinoid insecticides: *Biochemical Sites of Insecticide Action and Resistance* (Ed. I. Ishaaya), Springer-Verlag Berlin, Heidelberg, pp. 77-105 Date: 2001 non-GLP, published	no	-
A6.1.1/01	XXX	1997a	TI-435: Acute oral toxicity study in the rat. XXX, report no. 586/120-1032 SumiTake report no. DTOX003 September 18, 1997 GLP, unpublished	yes	SumiTake
A6.1.1/02*	XXX	1997b	TI-435: Acute oral toxicity study in the mouse. XXX, report no. 586/121-1032 SumiTake report no. DTOX004 September 18, 1997 GLP, unpublished	yes	SumiTake

A6.1.1/03*	XXX	2002	Original: An acute oral neurotoxicity study with technical grade TI-435 in Fischer 344 rats. Supplemental: An acute oral dose range-finding study with technical grade TI-435 in Fischer 344 rats. XXX Report no. 108960-2; 97-912-OE December 30, 2002 GLP, unpublished Original report no. 108960; 97-412-OH; 12.10.200	yes	SumiTake
A6.1.2/01*	XXX	1997c	TI-435: Acute dermal toxicity study in the rat. XXX, report no. 586/122-1032 SumiTake report no. DTOX005 June 25, 1997 GLP, unpublished	yes	SumiTake
A6.1.3/01*	XXX	1998	TI-435: Single dose inhalation (head-only) toxicity study in the rat. XXX, report no. 586/129-D6154 SumiTake report no. DTOX014 April 21, 1998 GLP, unpublished	yes	SumiTake
A6.1.4/01*	XXX	1997d	TI-435: Skin irritation study in the rabbit. XXX, report no. 586/124-1032 SumiTake report no. DTOX006 June 25, 1997 GLP, unpublished	yes	SumiTake
A6.1.4/02*	XXX	1997e	TI-435: Eye irritation study in the rabbit. XXX, report no. 586/123-1032 SumiTake report no. DTOX007 July 30, 1997 GLP, unpublished	yes	SumiTake
A6.1.5/01*	XXX	1997	TI-435: Skin sensitisation study in the guinea pig. XXX, report no. 586/125-1032 SumiTake report no. DTOX008 October 23, 1997 GLP, unpublished	yes	SumiTake
A6.10.1/01	Herbold, B.	2001	N-Methylnitroguanidin: Salmonella/microsome test – Plate incorporation and preincubation method. Bayer AG, report no. PH 30755; T00669528 February 21, 2001 GLP, unpublished	yes	SumiTake / Bayer
A6.10.1/02	XXX	2000c	TZNG: Acute oral toxicity study in the rat. XXX, report no. 586/163-D6144 SumiTake report no. DTOX025 January 20, 2000 GLP, unpublished	yes	SumiTake
A6.10.1/03	Dawkes, N.	1999c	TZNG: Reverse mutation in five histidine-requiring strains of *Salmonella typhimurium*. Covance, England, report no. 586/165-D5140 SumiTake report no. DTOX020 June 1999 GLP, unpublished	yes	SumiTake

A6.10.1/04	XXX	1999c	TMG: Acute oral toxicity study in the rat. XXX, report no. 586/164-D6144 SumiTake report no. DTOX022 July 1999 GLP, unpublished	yes	SumiTake
A6.10.1/05	Dawkes, N.	1999d	TMG: Reverse mutation in five histidine-requiring strains of *Salmonella typhimurium*. Covance, England, report no. 586/166-D5140 SumiTake report no. DTOX021 June 1999 GLP, unpublished	yes	SumiTake
AA6.10.2/ 01*	Unakami, S.	2000	Pharmacological studies on TI-435. Kashima Laboratory, Mitsubishi Chemical Safety Institute, Japan, report no. 9L668 SumiTake report no. DTOX049 January 20, 2000 GLP, unpublished	yes	SumiTake
A6.2*	XXX	2000d	[Nitroimino-^{14}C]- and [Thiazolyl-2-^{14}C]TI-435 toxicokinetic behaviour and metabolism in the rat including whole body autoradiography. report no. MR 348/00 SumiTake report no. DTOX062 October 11, 2000 GLP, unpublished	yes	SumiTake
A6.2/02*	XXX	2003	A study to determine the dermal absorption of TI 435 FS 600 when administered dermally to male Rhesus monkeys. XXX, report no. 200494 February 27, 2003 GLP, unpublished	yes	Bayer / SumiTake
A6.2/03	XXX	2003	XXX Absorption, tissue distribution, excretion, and metabolism of clothianidin in rats. XXX 51, 7066-7072	no	published
A6.3.1/01*	XXX	1997a	TI-435: Toxicity to mice by dietary administration for 4 weeks. XXX, report no. TDA 180/960497 SumiTake report no. DTOX002 February 19, 1997 GLP, unpublished	yes	SumiTake
A6.3.1/02*	XXX	2000	4-week dietary toxicity study with TI-435 in dogs. XXX, report no. 6155-106 SumiTake report no. DTOX026 February 1, 2000 GLP, unpublished	yes	SumiTake
A6.3.1/03	XXX	1997b	TI-435: Toxicity to rats by dietary administration for 4 weeks. XXX; report TDA 179/960496 SumiTake report no. DTOX001 February 19, 1997 GLP, unpublished	yes	SumiTake
A6.3.1/04	XXX	1998	Palatability pilot study for dietary concentrations of TI-435 in dogs. XXX, report no. 6155-107 SumiTake report no. DTOX015 May 1, 1998 non-GLP, unpublished	yes	SumiTake

A6.3.2/01*	XXX	2000	28-day dermal toxicity study with TI-435 in rats. XXX; report no. 6155-120 SumiTake report no. DTOX060 October 13, 2000 GLP, unpublished	yes	SumiTake
A6.4.1/01*	XXX	2000a	13-week dietary toxicity study with TI 435 in dogs. XXX, report no. 6155-111 SumiTake report no. DTOX033 March 14, 2000 GLP, unpublished	yes	SumiTake
A6.4.1/02	XXX	2000b	52-week dietary chronic toxicity study with TI-435 in dogs. XXX, report no. 6155-113 SumiTake report no. DTOX034 March 22, 2000 GLP, unpublished	yes	SumiTake
A6.4.1/03*	XXX	2000	Technical grade TI 435: A subchronic toxicity testing study in the rat. XXX, report no. 109075 SumiTake report no. DTOX043; 98-172-QO February 22, 2000 GLP, unpublished	yes	SumiTake
A6.4.1/04	XXX	2000a	TI-435: Toxicity to rats by dietary administration for 13 weeks. Final draft report. XXX, report no. TDA 194/962814 SumiTake report no. DTOX052 September 8, 2000 non-GLP, unpublished	yes	SumiTake
A6.4.1/05*	XXX	2000b	TI-435: Toxicity to mice by dietary administration for 13 weeks. Final draft report. XXX, report no. TDA 193/962813 SumiTake report no. DTOX053 September 8, 2000 non-GLP, unpublished	yes	SumiTake
A6.5*			see A6.7		
A6.6.1/01*	Thompson, P.W.	2000	TI-435: Reverse mutation assay “Ames test” using *Salmonella typhimurium* and *Escherichia coli*. Safepharm Lab. Ltd., report no. 178/110 SumiTake report no. DTOX035 March 8, 2000 GLP, unpublished	yes	SumiTake
A6.6.1/02*	Otsuka, M.	1990b	Bacterial reverse mutation test of TIR-435. Hita Research Lab. ,Chemical Biotesting Center, Chemicals Inspection & Testing Institute, report no. T-2276 SumiTake report no. DTOX047 April 23, 1990 GLP, unpublished	yes	SumiTake
A6.6.1/03*	Herbold, B.	1999a	TI 453 : Salmonella/microsome test plate incorporation and preincubation method. First version of Bayer AG, report no. 28849,	yes	SumiTake

			Revised version of Bayer AG, report no. 26584 SumiTake report no. DTOX041 June 16, 1999 GLP, unpublished		
A6.6.1/04*	Herbold, B.	1999b	TI 435: Salmonella/microsome test using *Salmonella typhimurium* TA 1535 plate incorporation and preincubation method. First version of Bayer AG, report no. 25739, First revision of Bayer AG, report no. 25739A SumiTake report no. DTOX042 May 31, 1999 GLP, unpublished	yes	SumiTake
A6.6.2/01*	Wright, N.P.	2000	TI-435: Chromosome aberration test in CHL cells *in vitro*. Safepharm Lab. Ltd., report no. 178/111 SumiTake report no. DTOX036 March 8, 2000 GLP, unpublished + Amendment 20.09.2000	yes	SumiTake
A6.6.3/01*	XXX	2000a	TI-435: L5178Y TK +/- mouse lymphoma assay. XXX., report no. 178/112 SumiTake report no. DTOX037 March 8, 2000 GLP, unpublished + Amendment 20.09.2000	yes	SumiTake
A6.6.3/02*	XXX	1999a	TI-435: Mutagenicity study for the detection of induced forward mutations in the V79-HPRT assay in vitro. First version of XXX, report no. 28851 Revised version XXX, report no. 26437. SumiTake report no. DTOX039 June 16, 1999 GLP, unpublished	yes	SumiTake
A6.6.4/01*	XXX	2000b	TI-435: Micronucleus test in the mouse. XXX., report no. 178/113 SumiTake report no. DTOX038 March 8, 2000 GLP, unpublished + Amendment 20.03.2000 / 29.09.2000	yes	SumiTake
A6.6.5/01*	XXX	(1999 b) 2001	TI 435: Test on unscheduled DNA synthesis with rat liver cells *in vivo*. 1st Amendment to report no. 28850 of 1999-06-16 XXX, report no. 28850A *replacing*: Revised version of XXX, report no. 26915 (raw data added) SumiTake report no. DTOX040 June 16, 1999 GLP, unpublished	yes	SumiTake
A6.7/01*	XXX	2000a	104-week dietary combined chronic toxicity and carcinogenicity study with TI-435 in rats. Volume I to XVI XXX report no. 6155-108 SumiTake report no. DTOX046 April 11, 2000	yes	SumiTake

			GLP, unpublished + Amendment 28.11.2000		
A6.7/02*	XXX	2000b	78-week dietary carcinogenicity study with TI-435 in mice. Volume I to VIII XXX, report no. 6155-109 SumiTake report no. DTOX045 March 27, 2000 GLP, unpublished + Amendment no.1 ;20.11.2000	yes	SumiTake
A6.8.1/01*	XXX	1998a	Oral (gavage) developmental toxicity study of TI-435 in rats. XXX, report no. 1120-001 SumiTake report no. DTOX009 April 14,1998 GLP, unpublished	yes	SumiTake
A6.8.1/02*	XXX	1998b	Oral (stomach tube) developmental toxicity study of TI-435 in rabbits. XXX, report no. 1120-002 SumiTake report no. DTOX013 April 16,1998 GLP, unpublished	yes	SumiTake
A6.8.2	Bray, C.; Son, J.H.; Kumar, P.; Meizel, S.	2005	Mice deficient in CHRNA7, a subunit of the nicotinic acetylcholine receptor, produce sperm with impaired motility. Biology of Reproduction 73, 807-814 No GLP, published	no	Public domain
A6.8.2	Kumar, P.; Meizel, S.	2005	Nicotinic acetylcholine receptor subunits and associated proteins in human sperm. Journal of Biological Chemistry 280, 25928-25935 No GLP, published	no	Public domain
A6.8.2	Palmero, S.; Bardi, B.; Coniglio, L.; Falugi, C.	1999	Presence and localization of molecules related to the cholinergic system in developing rat testis. European Journal of Histochemistry 43, 277-283 No GLP, published	no	Public domain
A6.8.2*	XXX	2000	A two generation reproductive toxicity study with TI-435 in the Sprague-Dawley rat. XXX, report no. 109282 SumiTake report no. DTOX044; 98-672-PF March 27, 2000 GLP, unpublished + Supplement; 109282-2; 12.03.2003	yes	SumiTake
A6.9/01*	XXX	2000	An acute oral neurotoxicity screening study with technical grade TI-435 in Fischer 344 rats. XXX, report no. 108960 SumiTake report no. DTOX057; 97-412-OH, October 12, 2000 GLP, unpublished	yes	SumiTake
A6.9/02*	XXX	2000	A special acute oral neurotoxicity study to establish a no-observed-effect-level with technical grade TI-435 in Fischer 344 rats. (Supplemental study to original study: An acute	yes	SumiTake

			oral neurotoxicity screening study with technical grade TI-435 in Fischer 344 rats. SumiTake report no. DTOX059 XXX report no. 108960-1; October 12, 2000 (original), November 8, 2000 (supplemental study); 00-N12-BA; 99-N12-BA GLP, unpublished		
A6.9/03*	XXX	2000	A subchronic neurotoxicity screening study with technical grade TI-435 in Fischer 344 rats. SumiTake report no. DTOX058 XXX, report no. 109400; 97-472-OM October 12, 2000 GLP, unpublished	yes	SumiTake
A6.9/04*	XXX	2000	Developmental neurotoxicity study of TI-435 administered orally via the diet to Crl:CD BR VAF/Plus presumed pregnant rats. XXX, report no.1120-003 SumiTake report no. DTOX061 October 20, 2000 GLP, unpublished + Amendment no. 1; 14.02.2001	yes	SumiTake
A7.1.1.1.1/01*	Lewis, C.J.	2000a	(^{14}C)-TI-435: Hydrolytic stability.Covance Ltd., report no. 586/140-D2142 SumiTake report no. DEFT012 June 5, 2000 GLP, unpublished	yes	SumiTake
A7.1.1.1.2/01*	Babczinski, P.; Bornatsch, W.	2000	Photolysis of [nitroimino-^{14}C]TI-435 and [thiazolyl-2-^{14}C]TI-435 in sterile aqueous buffer solution.Bayer AG, report no. MR-248/00 SumiTake report no. DEFT023 September 19, 2000 GLP, unpublished	yes	SumiTake
A7.1.1.1.2/02	Schad, T.	2000a	Calculation of half-lives of TI-435 and its main metabolites generated by photolysis in sterile aqueous buffer solution.Bayer AG, report no. MR-121/00 SumiTake report no. DEFT015 April 19, 2000 GLP, unpublished	yes	SumiTake
A7.1.1.1.2/03	Babczinski, P.	2000	Photolysis of TI-435 in natural US-water.Bayer AG, report no. MR 391/00 (BCP 79) SumiTake report no. DEFT031 December 7, 2000 GLP, unpublished	yes	SumiTake

A7.1.1.1.2/04	Schad, T.	2000b	Calculation of half-lives of TI-435 and its main metabolites generated by photolysis in natural water.Bayer AG, report no. MR-204/00 SumiTake report no. DEFT009 April 14, 2000 GLP, unpublished	yes	SumiTake
A7.1.1.1.2/05	Hellpointner, E.	1999a	Determination of the quantum yield and assessment of the environmental half-life of the direct photodegradation of TI-435 in water.Bayer AG, report no. MR-360/99 SumiTake report no. DEFT005 August 2, 1999 GLP, unpublished	yes	SumiTake
A7.1.1.2.1/01*	Bealing, D.J.; Watson, S.	1999	TI-435: Assessment of ready biodegradability by measurement of carbon dioxide evolution.Covance, report no. 586/162-D2145 SumiTake report no. DEFT004 December 1999 GLP, unpublished	yes	SumiTake
A7.1.2.2.2/01	Gilges, M.; Brumhard, B.	2000	see A7.1.2/01		
A7.1.2.2.2/02	Reddemann, J.	2000	see A7.1.2/02		
A7.1.2/01*	Gilges, M.; Brumhard, B.	2000	Aerobic degradation and metabolism of TI-435 in the water/sediment system.Bayer AG, report no. MR-505/99SumiTake report no. DEFT011 April 14, 2000 Amendment no. 1 of April 14, 2001 GLP, unpublished	yes	SumiTake
A7.1.2/02*	Reddemann, J.	2000	Anaerobic aquatic metabolism of the active ingredient TI-435.Bayer AG, report no. MR-497/00SumiTake report no. DEFT032 December 13, 2000 Amendment no. 1 of April 9, 2001 GLP, unpublished	yes	SumiTake
A7.1.3/01*	Lewis, C.J.	2000b	[^{14}C]TI-435: Adsorption/desorption in soil.Covance, report no. 586/139-D2142 SumiTake report no. DEFT013 August 17, 2000 GLP, unpublished	yes	SumiTake
A7.1.3/02	Stupp, H.P.	2001a	Time-dependent sorption of TI-435 in two different soils.Bayer AG, report no. MR-518/00 SumiTake report no. DEFT035 January 17, 2001 GLP, unpublished	yes	SumiTake

A7.2.1/01*	Gilges, M.	2000	Aerobic degradation and metabolism of TI-435 in four soils.Bayer AG, report no. MR-497/99 SumiTake report no. DEFT010 March 13, 2000 Amendment no. 1 of April 9, 2001 GLP, unpublished	yes	SumiTake
A7.2.1/02*	Schad, T.	2000c	Aerobic degradation and metabolism of TI-435 in six soils. Bayer AG, report no. MR-419/99 SumiTake report no. DEFT014 July 31, 2000 Amendment no. 1 of April 9, 2001 GLP, unpublished	yes	SumiTake
A7.2.2.1/01	Gilges, M.	2000	see A7.2.1/01		
A7.2.2.1/02	Schad, T.	2000c	see A7.2.1/02		
A7.2.2.2/01*	Schramel, O.	2000b	Dissipation of TI-435 (600 FS) in soil under field conditions (France, Germany, Great Britain).Bayer AG, report no. RA-2065/98 SumiTake report no. DEFT018 October 20, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.2.2.2/02	Schramel, O.	2000c	Dissipation of TI-435 (600 FS) in soil under field conditions (Northern France, Great Britain).Bayer AG, report no. RA-2066/98 SumiTake report no. DEFT019 October 20, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.2.2.2/03	Schramel, O.	2000d	Dissipation of TI-435 (600 FS) in soil under field conditions (Southern France, Spain). Bayer AG, report no. RA-2067/98 SumiTake report no. DEFT02 0October 20, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.2.2.2/04	Schad, T.	2000d	Calculation of half-lives of TI-435 based on field dissipation studies.Bayer AG, report no. MR-414/00 SumiTake report no. DEFT021 September 20, 2000 GLP, unpublished	yes	SumiTake
A7.2.2.2/05	Schramel, O.	2001	Determination of the storage stability of TI-435 and of the metabolites TZNG, TZMU, TMG and MNG in soil.Bayer AG, report no. MR-477/01 SumiTake report no. DEFT041 November 5, 2001 GLP, unpublished	yes	SumiTake /Bayer

A7.2.2.2/06	Stupp, H.-P., Fahl, U.	2003	Plfanzenschutz-Nachrichten, Bayer 56/2003, I: Environmental fate of clothianidin (TI-435, Poncho®), page 59-74		
A7.2.2.4/01*	Dorn, R.	2000	Degradation of ^{14}C-MNG, a degradate of TI-435, in three different soils. SLFA Neustadt, report of study no. TAK06 SumiTake report no. DEFT029 December 19, 2000	yes	SumiTake
A7.2.2.4/02	Hein, W.	2000	Degradation of ^{14}C-TZNG, a degradate of TI-435, in three different soils. SLFA Neustadt, report of study no. TAK05 SumiTake report no. DEFT028 December 19, 2000	yes	SumiTake
A7.2.2.4/03	Hellpointner, E.	1999b	Photolysis of [Guanidine-^{14}C]TI-435 on soil surface.Bayer AG, report no. MR-154/99 SumiTake report no. DEFT006 August 30, 1999GLP, unpublished	yes	SumiTake
A7.2.3.1/01	Dorn, R.;Hein, W.	2000a	Adsorption/desorption of ^{14}C-MNG, a degradate of TI-435, on five different soils.SLFA Neustadt, report of study no. TAK02 SumiTake report no. DEFT025 December 19, 2000 GLP, unpublished	yes	SumiTake
A7.2.3.1/02	Möndel, M.;Hein, W.	2000	Adsorption/desorption of ^{14}C-TZNG, a degradate of TI-435, on five different soils.SLFA Neustadt, report of study no. TAK01 SumiTake report no. DEFT024 December 19, 2000 GLP, unpublished	yes	SumiTake
A7.2.3.1/03	Dorn, R.;Hein, W.	2000b	Adsorption/desorption of ^{14}C-TZMU, a degradate of TI-435, on five different soils.SLFA Neustadt, report of study no. TAK03 SumiTake report no. DEFT026 December 19, 2000 GLP, unpublished	yes	SumiTake
A7.2.3.1/04	Dorn, R.;Hein, W.	2000c	Adsorption/desorption of ^{14}C-TMG, a degradate of TI-435, on five different soils.SLFA Neustadt, report of study no. TAK04 SumiTake report no. DEFT027 December 19, 2000 GLP, unpublished	yes	SumiTake

A7.2.3.2/01*	Stupp, H.P.	2001b	Degradation and translocation behavior of the insecticide active ingredient TI-435 under field conditions in a lysimeter (autumn application).Bayer AG, report no. MR-051/01 SumiTake report no. DEFT037 February 28, 2001 GLP, unpublished	yes	SumiTake /Bayer
A7.2.3.2/02*	Stupp, H.P.	2001c	Degradation and translocation behavior of the insecticide TI-435 in a lysimeter under field conditions.Bayer AG, report no. MR-599/00 SumiTake report no. DEFT036 March 16, 2001 GLP, unpublished	yes	SumiTake /Bayer
A7.3.1/01*	Hellpointner, E.	1998	Calculation of the chemical lifetime of TI-435 in the troposphere.Bayer AG, report no. MR-705/98 SumiTake report no. DEFT008 September 9, 1998 non-GLP, unpublished	yes	SumiTake
A7.4.1.1/01*	XXX	1998a	TI-435 technical, fish (Rainbow trout), acute toxicity test, 96 h, limit test. XXX no. 970714TA/FAR54472/CFF54472 SumiTake report no. DECO002 January 6, 199 8 GLP, unpublished	yes	SumiTake
A7.4.1.1/02	XXX	2000a	TI-435 technical: A 96-hour static acute toxicity test with the bluegill (Lepomis macrochirus). XXX, report no. 110003/149A-123 SumiTake report no. DECO056 October 27, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.1/03	XXX	2000	N-Methylnitroguanidine - Acute toxicity (96 hours) to Rainbow trout (Oncorhynchus mykiss) in a static test (limit test). XXX, report no. DOM 20038 SumiTake report no. DECO069 October 5, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.1/04	XXX	2000a	TI 435-Thiazolylnitroguanidine - Acute toxicity (96 hours) to Rainbow trout (Oncorhynchus mykiss) in a static test (limit test). XXX, report no. DOM 20039 SumiTake report no. DECO070 September 14, 2000 GLP, unpublished	yes	SumiTake /Bayer

A7.4.1.1/05	XXX	2000b	TI 435-thiazolylmethylguanidine – Acute toxicity (96 hours) to Rainbow trout (Oncorhynchus mykiss) in a static test (limit test). Version 3. XXX, report no. DOM 20040 SumiTake report no. DECO068 September 14, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.2/01	Palmer, S.J.; MacGregor, J.A.; Krueger, H.O.	2000b	TI-435 Technical: A 48-hour static acute toxicity test with the cladoceran (Daphnia magna).Wildlife International, report no. 110004/149A-122 SumiTake report no. DECO057 Date: October 27, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.2/02*	Noack, M.;Geffke, T.	1997	TI-435 technical - Acute immobilisation test (48 h) to Daphnia magna STRAUS. Dr.U.Noack-Laboratorium, study no. DAI54471 (inlife part) project no. 970714TA SumiTake report no. DECO001 December 15, 1997, amended December 15, 2000 GLP, unpublished	yes	SumiTake
A7.4.1.2/03	Hendel, B.	2000a	Acute toxicity of N-methylnitroguanidine (techn.) to water fleas (Daphnia magna).Bayer AG, report no. HDB/Dm 232 SumiTake report no. DECO072 September 22, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.2/04	Hendel, B.	2000b	Acute toxicity of TI 435-thiazolylnitro-guanidine (techn.) to water fleas (Daphnia magna).Bayer AG, report no. HDB/Dm 231 SumiTake report no. DECO073 September 22, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.2/05	Hendel, B.	2000c	Acute toxicity of TI 435-thiazolylmethyl-guanidine (techn.) to water fleas (Daphnia magna).Bayer AG, report no. HDB/Dm 229 SumiTake report no. DECO071 September 22, 2000 GLP, unpublished	yes	SumiTake /Bayer

A7.4.1.3/01*	Sutherland, C.A.; MacGregor, J.A.; Krueger, H.O.	2000	TI-435 technical: A 5-day toxicity test with the freshwater alga (Selenastrum capricornutum).Wildlife International, report no. 197A-102 SumiTake report no. DECO051 October 27, 2000 GLP, unpublished	yes	SumiTake
A7.4.1.3/02	Wilhelmy, H.; Geffke, T.	1998b	TI-435 technical, Alga, growth inhibition test (120 [h]).Dr. U. Noack-Laboratorium project no. 970714TA/SSO54471/CSO54471 SumiTake report no. DECO004 January 6, 1998 GLP, unpublished	yes	SumiTake
A7.4.1.3/03	Dorgerloh, M.	2000c	N-methylnitroguanidine – Influence on the growth of green alga, Selenastrum capricornutum.Bayer AG; report no. DOM 20035 SumiTake report no. DECO075 September 27, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.3/04	Dorgerloh, M.	2000d	TI 435-thiazolylnitroguanidine – Influence on the growth of green alga, Selenastrum capricornutum.Bayer AG; report no. DOM 20036 SumiTake report no. DECO076 October 5, 200 0GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.3/05	Dorgerloh, M.	2000e	TI 435-Thiazolylmethylguanidine - Influence on the growth of the green alga, Selenastrum capricornutum. Version 2.Bayer AG; report no. DOM 20037 SumiTake report no. DECO074 September 29, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.4/01*	Bealing, D.J.; Watson, S.	2000	TI-435 technical: Determination of inhibition of respiration of activated sludge.Covance Laboratories, report no. 586/210-D2145 SumiTake report no. DECO045 June 30, 2000 GLP, unpublished	yes	SumiTake

A7.4.3.2/01*	XXX	2000	TI-435 Technical: An early life-stage toxicity test with the fathead minnow (Pimephales promelas). XXX, report no.110163/149A-124B SumiTake report no. DECO059 Date: December 13, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.3.4/01*	Noack, M.; Geffke, T.	1998	TI-435 technical: Daphnia magna reproduction test (21d).Dr. Noack-Laboratorium, project no. 970714TA/DRE54471/CDR54471 SumiTake report no. DECO010 June 4, 1998 GLP, unpublished	yes	SumiTake
A7.4.3.5.1/01*	Heimbach, F.	1999	Influence of TI-435 technical on development and emergence of larvae of Chironomus riparius in a water-sediment system.Bayer AG; report no. HBF/Ch 28 SumiTake report no. DECO018 April 30, 1999 GLP, unpublished	yes	SumiTake
A7.4.3.5.1/02	Heimbach, F.	1998	Influence of TMG (tech.) on development and emergence of larvae of Chironomus riparius in a water-sediment system.Bayer AG; report no. HBF/Ch 26 SumiTake report no. DECO014 December 15, 1998 GLP, unpublished	yes	SumiTake
A7.4.3.5.1/03	Mattock, S.D.	2001	TI-435: comparative acute toxicity of Chironomus riparius with TZMU, MU, TZNG and MNG.Covance Laboratories, report no. 586/218-D2145 SumiTake report no. DECO064 January 9, 2001 GLP, unpublished	yes	SumiTake
A7.4.3.5.2/01	Palmer, S.J.; MacGregor, J.A.; Krueger, H.O.	2000c	TI-435 technical: A 14-day static-renewal toxicity test with duckweed (Lemna gibba G3).Wildlife International, report no. 110005/149A-125 SumiTake report no. DECO058 October 30, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.3.6/01*	Memmert, U.	2001	Fate and ecological effects of TI-435 50 WG in an outdoor freshwater mesocosm study.RCC Ltd., report no. 753851 SumiTake report no. DECO082 March 14, 2001 GLP, unpublished	yes	SumiTake

A7.5.1.1/01*	Keirs, D.C.; Caley, C.Y.	1999	The effect of TI-435 50% WDG on soil microflora.Inveresk Research, report no. 17938 SumiTake report no. DECO 030 December 7, 1999 GLP, unpublished	yes	SumiTake
A7.5.1.1/02*	Anderson, J.P.E.	2000a	Influence of the metabolite N-methyl-nitro-guanidine on the microbial mineralization of nitrogen in soils.Bayer AG; report no. AJO/213200 SumiTake report no. DECO079 October 16, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.5.1.1/03	Anderson, J.P.E.	2000b	Influence of the metabolite TI-435-thiazolylnitroguanidine on the microbial mineralization of nitrogen in soils.Bayer AG; report no. AJO/213100 SumiTake report no. DECO078 October 16, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.5.1.1/04	Anderson, J.P.E.	2000c	Influence of the metabolite TI-435-thiazolylmethylguanidine on the microbial mineralization of nitrogen in soils.Bayer AG; report no. AJO/213000 SumiTake report no. DECO077 October 16, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.5.1.2/01*	Weyman, G.S.	1998	TI-435 technical: Acute toxicity to the earthworm Eisenia foetida.Covance Laboratories, report no. 586/136-1018SumiTake report no. DECO005 February 23, 1998 GLP, unpublished	yes	SumiTake
A7.5.1.2/02	Dechert, G.	2000	TI-435 a.i.: Inhibition of reproduction of collembola (Folsomia candida).Dr. U. Noack-Laboratorium; report of project no. 991207BK SumiTake report no. DECO083 October 25, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.5.1.2/03	Noack, M.	2000a	MNG - Earthworm (Eisenia foetida), acute toxicity test in artificial soil.Dr. Noack-Laboratorium, report no. RRA66531 SumiTake report no. DECO050 October 23, 2000 GLP, unpublished	yes	SumiTake

A7.5.1.2/04	Noack, M.	2000b	TZNG - Earthworm (Eisenia foetida), acute toxicity test in artificial soil.Dr. Noack-Laboratorium, report no. RRA66521 SumiTake report no. DECO049 October 23, 2000 GLP, unpublished	yes	SumiTake
A7.5.1.2/05	Moser, Th.;Römbke, J.	2001a	Acute and reproduction toxicity of N-Methylnitroguanidine to the collembolan species Folsomia candida according to the ISO Guideline 11267 “Soil Quality - Inhibition of reproduction of Collembola (Folsomia candida) by soil pollutants” (1999).ECT Oekotoxikologie GmbH, report of study no. P3CR SumiTake report no. DECO084 February 6, 2001 GLP, unpublished	yes	SumiTake /Bayer
A7.5.1.2/06	Moser, Th.;Römbke, J.	2001b	Acute and reproduction toxicity of TI 435 – Thiazolylnitroguanidine to the collembolan species Folsomia candida according to ISO Guideline 11267 "Soil Quality – Inhibition of reproduction of Collembola (Folsomia candida) by soil pollutants" (1999).ECT Oekotoxikologie GmbH, report of study no. P4CR SumiTake report no. DECO085 February 6, 2001 GLP, unpublished	yes	SumiTake /Bayer
A7.5.1.3/01*	Brignole, A.J.; Porch, J.R.; Krueger, H.O.	2000	TI-435 50% WDG: A toxicity test to determine the effects of the test substance on seedling emergence of ten species of plants.Wildlife International, Ltd., report of project no. 197-126 SumiTake report no. DECO052 October 26, 2000GLP, unpublished	yes	SumiTake
A7.5.1.3/02*	Brignole, A.J.;Porch, J.R.;Krueger, H.O.;Kendall, T.Z.	2000	TI-435 50% WDG: A toxicity test to determine the effects of the test substance on vegetative vigor of ten species of plants.Wildlife International, report of project no. 197-127 SumiTake, report no. DECO053 October 26, 2000 GLP, unpublished	yes	SumiTake

A7.5.2.1/01*	Wachter, S.	1999	TI-435 50% WDG: Assessment of sublethal effects on Eisenia foetida in artificial soil (Determination of effects on reproduction).Arbeitsgemeinschaft GAB Biotechnologie GmbH & IFU Umweltanalytik GmbH, report of study no. 99209/01-NREf SumiTake report no. DECO034 October 6, 1999GLP, unpublished	yes	SumiTake
A7.5.2.1/02*	Dechert, G.	2000	see A7.5.1.2/02		
A7.5.2.1/03	Moser, Th.;Römbke, J.	2001a	see A7.5.1.2/05		
A7.5.2.1/04	Moser, Th.;Römbke, J.	2001b	see A7.5.1.2/06		
A7.5.2.2/01	Brignole, A.J.; Porch, J.R.; Krueger, H.O.	2000	see A7.5.1.3/01		
A7.5.2.2/02	Brignole, A.J.;Porch, J.R.;Krueger, H.O.;Kendall, T.Z.	2000	see A7.5.1.3/02		
A7.5.3.1.1/01	XXX	1998a	TI-435 technical acute oral toxicity (LD_{50}) to Bobwhite quail. XXX, report no. TDA 232/973538 SumiTake report no. DECO008 June 1, 1998GLP, unpublished	yes	SumiTake
A7.5.3.1.1/02	XXX	1999	TI-435 technical: An acute oral toxicity study with the Japanese quail. XXX, report no. 197-128 SumiTake report no. DECO033 January 6, 2000GLP, unpublished	yes	SumiTake
A7.5.3.1.2/01	XXX	1998b	TI-435 technical: Dietary LC_{50} to the Bobwhite quail. XXX, report no. TDA 233/973539 SumiTake report no. DECO007 March 20, 1998GLP, unpublished	yes	SumiTake

A7.5.3.1.2/02	XXX	1998c	TI-435 technical: Dietary LC_{50} to the Mallard duck. XXX, report no. TDA 234/973540SumiTake report no. DECO009June 1, 1998GLP, unpublished	yes	SumiTake
A7.5.3.1.3/01	XXX	2000a	TI-435 technical: A reproduction study with the Northern Bobwhite (Colinus virginianus). XXX, report no. 197-122SumiTake report no. DECO031January 17, 2000GLP, unpublished	yes	SumiTake
A7.5.3.1.3/02	XXX	2000b	TI-435 technical: A reproduction study with the Mallard (Anas platyrhynchos). XXX, report no. 197-123 SumiTake report no. DECO032January 17, 2000GLP, unpublished	yes	SumiTake
B3.1 B3.4 B3.5 B3.6 B3.7 **B3.10** **B3.11**	Warncke, U.	2003	Determination of physical-chemical properties of the test item SPU-01850-I-0-SL Laboratory: Spiess-Urania Chemicals GmbH - Versuchsstation Christinenthal Doc. No.: U03PCI02 Date: 03.12.2003 GLP: yes; not published	yes	SPU
B3.2	Warncke, U.	2003	Explosive properties of SPU-01850-I-0-SL EEC method A.14 Laboratory: Spiess-Urania Chemicals GmbH - Versuchsstation Christinenthal Doc. No.: Wa-250803-01850 Date: 25.08.2003; not published	yes	SPU
B4.1	Warncke, U., Lüdke, S.	2003	Validated method of analysis for the determination of clothianidine (TI-435) in SPU-01850-I-0-SL Laboratory: Spiess-Urania Chemicals GmbH - Versuchsstation Christinenthal Doc. No.: Wa-29-10-03-1850 Date: 06.10.2003; not published	yes	SPU
B5.10 /01	Schumacher, P., Fennert, E.-M.	2003	Determination of toxic values against Reticulitermes santonensis De Feytaud according to EN 117 (08/90) - without accelerated ageing procedure - SPU-01680-I Laboratory: Materialprüfungsamt des Landes Brandenburg Doc. No.: 3.2/02/8390/01 Date: 19.02.2003; not published	yes	SPU

B5.10 /02	Schumacher, P., Fennert, E.-M.	2003	Determination of toxic values against Reticulitermes santonensis santonensis De Feytaud according to EN 117 (08/90) after leaching procedure according to EN 84 (05/97) - SPU-01680-I Laboratory: Materialprüfungsamt des Landes Brandenburg Doc. No.: 3.2/02/8390/02 Date: 24.03.2003; not published	yes	SPU
B5.10 /03	Schumacher, P., Fennert, E.-M.	2003	Determination of the toxic values against larvae of Hylotrupes bajulus (L) according to EN 47 (08/90) - without accelerated ageing procedure - SPU-01680-I Laboratory: Materialprüfungsamt des Landes Brandenburg Doc. No.: 3.2/02/8390/03 Date: 25.02.2003; not published	yes	SPU
B5.10 /04	Schumacher, P., Fennert, E.-M.	2003	Determination of the toxic values against larvae of Hylotrupes bajulus (L) according to EN 47 (08/90) after leaching procedure according to EN 84 (05/97) - SPU-01680-I Laboratory: Materialprüfungsamt des Landes Brandenburg Doc. No.: 3.2/02/8390/04 Date: 02.05.2003; not published	yes	SPU
B5.10 /05	Schumacher, P., Fennert, E.-M.	2004	Peer review - Statement about the protective effectiveness of SPU-01680-I (Clothianidin, TI-435) against wood destroying insects Laboratory: Materialprüfungsamt des Landes Brandenburg Doc. No.: 3.2/04/8553/01 Date: 18.02.2004; not published	yes	SPU
B5.10 /06	Schumacher, P., Fennert, E.-M.	2005	Determination of the eradicate action against larvae of *Hylotrupes bajulus* (L.) according to ENV 1390 (05/95). Laboratory: Materialprüfungsamt des Landes Brandenburg, Eberwalde, Germany, Report no. 32/04/8595/01, Date: 21.03.2005; not published.	yes	SPU
B 6.1.1*	XXX	*2003*	*Acute Toxicity Study of SPU-01850-I by Oral Administration to CD Rats - Limit Test* *Laboratory* XXX *Doc. No.: 16762/03* *Date: 06.08.2003* *GLP: yes; not published*	*yes*	*SPU*
B 6.1.2*	XXX	*2003*	*Acute Toxicity Study of SPU-01850-I in Rats by Dermal Administration - Limit Test* *Laboratory:* XXX *Doc. No.: 16763/03* *Date: 25.08.2003* *GLP: yes; not published*	*yes*	*SPU*
B 6.2*/01**	XXX	*2003*	*Acute Skin Irritation Test (Patch Test) of SPU-01850-I in Rabbits* *Laboratory* XXX *Doc. No.: 16764/03* *Date: 06.08.2003* *GLP: yes; not published*	*yes*	*SPU*

B 6.2*I02**	XXX	*2003*	*Acute Eye Irritation Study of SPU-01850-I by Instillation into the Conjunctival Sac of Rabbits Laboratory* XXX *Doc. No.: 16765/03* *Date: 13.10.2003* *GLP: yes; not published*	*yes*	*SPU*
B 6.3*	XXX	*2003*	*Examination of SPU-01850-I in a Skin Sensitisation Test in Guinea Pigs According to Magnusson and Kligman (Maximisation Test)* *Laboratory:* XXX *Doc. No.: 16766/03* *Date: 13.10.2003* *GLP: yes; not published*	*yes*	*SPU*
B 7.1 /01	Marx, H.-N.	2003	Expert statement / Indication of leaching / Pressure treatment / TI-435 (active ingredient) preparation for wood protection Laboratory: SVB Marx Doc. No.: 01850-IIB-71a Date: 15.03.2004; not published	yes	SPU
B 7.1 /02	Marx, H.-N.	2003	Expert statement / Indication of leaching / Dipping treatment / TI-435 (active ingredient) preparation for wood protection Laboratory: SVB Marx Doc. No.: 01850-IIB-71b Date: 15.03.2004; not published	yes	SPU
B 7.1 /03	Schumacher P., Wegner, R.	2004	Testing of the preservative according OECD guideline for testing chemical (proposal for a new guideline I): Estimation of emission from preservative-treated wood to the environment: Laboratory method for wood held in storage after treatment and for wooden commodities that are not covered, and are not in contact with ground. Laboratory: Materialprüfungsamt des Landes Brandenburg, Eberswalde, Germany Doc. No.: 31/04/7447/02 Date: August 19, 2004; not published	yes	SPU
B 7.1 /04	Schumacher P., Wegner, R.	2004	Testing of the preservative according OECD guideline for testing chemical (proposal for a new guideline I): Estimation of emission from preservative-treated wood to the environment: Laboratory method for wood held in storage after treatment and for wooden commodities that are not covered, and are not in contact with ground. Laboratory: Materialprüfungsamt des Landes Brandenburg, Eberswalde, Germany Doc. No.: 31/04/7447/01 Date: August 19, 2004; not published	yes	SPU
B 7.7.1.1.1	XXX	2003	Fish (Rainbow trout), Acute Toxicity Limit Test, Static, 96 h SPU-01850-I-0-SL Laboratory: XXX Doc. No.: FAR92231 Date: 07.10.2003 GLP: yes; not published	yes	SPU

B 7.7.1.1.2	Noack, M.	2003	Acute Immobilisation Test (48 h) to Daphnia magna STRAUS, Limit-Test SPU-01850-I-0-SL Laboratory: Dr.U.Noack-Laboratorien Doc. No.: DAI92231 Date: 07.10.2003 GLP: yes; not published	yes	SPU
B 7.7.1.1.3	Scheerbaum, D.	2003	Alga, Growth Inhibition Test with Desmodesmus subspicatus, 72 h (formerly Scenedesmus subspicatus) SPU-01850-I-0-SL Laboratory: Dr.U.Noack-Laboratorien Doc. No.: SSO92231 Date: 07.10.2003 GLP: yes; not published	yes*	SPU