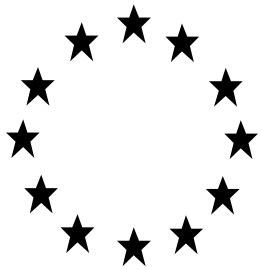
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Clothianidin

Product-type 18
(Insecticides, Acaricides and Products to control other Arthropods)

October 2014

Germany

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1 Procedure followed

This assessment report has been established as a result of the evaluation of the active substance clothianidin as product-type 18 (insecticides, acaricides and products to control other arthropods) carried out in the context of the work programme for the review of existing active substances provided for in Article 89 of Regulation (EU) No 528/2012, with a view to the possible approval of this substance.

Clothianidin (CAS no. 210880-92-5) was notified as an existing active substance, by Sumitomo Chemical Company Ltd., United Kingdom, hereafter referred to as the applicant, in product-type 18.

Commission Regulation (EC) No 1451/2007 of 4 December 2007[1] lays down the detailed rules for the evaluation of dossiers and for the decision-making process.

In accordance with the provisions of Article 7(1) of that Regulation, Germany was designated as Rapporteur Member State to carry out the assessment based on the dossier submitted by the applicant. The deadline for submission of a complete dossier for clothianidin as an active substance in Product Type 18 was 30 April 2006, in accordance with Annex V of Regulation (EC) No 1451/2007.

On 28 April 2006 und 29 April 2006, 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 30 October 2006.

On 27 May 2009, the Rapporteur Member State submitted to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the European Commission and the Agency. Revisions agreed upon on the Technical Meeting II/2010 were presented at the Biocidal Products Committee and the competent authority report was amended accordingly.

1.2 Purpose of the assessment report

The aim of the assessment report is to support the opinion of the Biocidal Products Committee and a decision on the approval of clothianidin for product-type 18 and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions

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

of this assessment report, which is available from the Agency website, shall be taken into account.

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

2. OVERALL SUMMARY AND CONCLUSIONS

2.1 Presentation of the Active Substance

2.1.1 Identity, Physico-Chemical Properties & Methods of Analysis

Identity, Physico-chemical Properties and Method of Analysis of Clothianidin:

The evaluation has established that for the active substance notified by Sumitomo Chemical Takeda Agro Company (now Sumitomo Chemical Company Ltd., United Kingdom), none of the manufacturing impurities considered are, based on information currently available, of toxicological or environmental concern.
Due to the comments made on the draft final CAR in 2014 it was decided to amend the identity of the active substance based on the results of the batch analysis, which resulted in a lower purity of the active substance. Therefore, the exposure calculations presented in the CAR can be regarded as worst case. All manufacturing impurities (except one) have lower or equal contents than those originally proposed as specification.
Clothianidin belongs to the chemical class of chloronicotinyls or neonicotinoids and is transformation product of Thiamethoxam during aerobic degradation in soil. It is a clear and colourless, solid powder. Its vapour pressure and volatility are very low. Clothianidin is a basic substance, which 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 with regard to physical/chemical data.
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.
In the frame of product authorisation, 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.

Residue analysis

Analytical methods for detection and identification are available for the active substance and, where relevant, for its metabolites, in soil, water, air and plant materials. In addition, validated confirmatory methods for these matrices were presented.

Identity, Physico-chemical Properties and Method of Analysis of SPU-02000-I-SC:

SPU-02000-I is a white and odourless paste. Due to the nature of the biocidal product,

SPU-02000-I-SC is not expected to exhibit any hazardous physical-chemical properties.

Residue analysis

As no relevant residues from the application of the active substance are expected, the same applies to the non-active ingredient of the product. No methods for the determination of residues of the product or its non-active ingredient are necessary.

2.1.2 Intended Uses and Efficacy

Clothianidin belongs to the chemical class of insecticides known as neonicotinoids or chloronicotinyls, which interfere with the nicotinic acetylcholine receptors at the postsynaptic membrane. The compound acts agonistically on insect nicotinic acetylcholine receptors located in the central nervous system. Clothianidin has an insecticidal effect by contact and ingestion (systemic insecticide).

Products in PT 18 containing clothianidin are intended for use in paint-on formulations for controlling insects such as houseflies (Musca spp) in animal housings and private households.

Evaluation of the submitted data under Directive 98/8/EEC resulted in the following statement:

Clothianidin has innate efficacy against adult flies (Musca spp) at the following concentrations and formulations:

Application by painting: 26 g a.i /L.

Application by spraying: 8.7 g a.i /L.

The efficacy rate increases during the first 3 days after application due to the mode of action of bait formulations (systemic effects after ingestion). The efficacy after a single application has been demonstrated for a time period of 8 weeks under laboratory conditions in simulated-use-trials. The length of time of residual effect has to be confirmed for product authorisation by field studies.

Occurrence of Resistance

Resistance and cross-resistance against neonicotinoids (chloronicotinyls like thiamethoxam, acetamiprid and imidacloprid), a group of insecticides acting agonistically on insect nicotinic acetylcholine receptors (nAChRs) can occur in relevant susceptible pests in Europe. In general, precautions should be taken to reduce the possibility of insects developing resistance to neonicotinoid insecticides.

For the intended uses as a biocidal product, SPU-02000-I-SC as PT 18 should only be used against adult insects (e.g. *Musca domestica* and *Musca autumnalis*) and is not applicable for other stages (e.g. eggs, larvae and pupae). The application as a paste formulation takes place above the lethal level. Therefore, it is expected that development of resistance in target insects does not occur. In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.3 Classification and Labelling

Classification and Labelling of Clothianidin

Proposed classification as in the COMMISSION DIRECTIVE 2009/2/EC of 15 January 2009 amending, for the purpose of its adaptation to technical progress, for the 31st time, Council Directive 67/548/EEC:

Table 2-1 Proposed classification based on Directive 67/548/EEC

Classification		
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 COMMISSION DIRECTIVE 2009/2/EC of 15 January 2009 amending, for the purpose of its adaptation to technical progress, for the 31st time, Council Directive 67/548/EEC the same classification was proposed.

According to *COMMISSION REGULATION (EC) No 790/2009 of 10 August 2009 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures*, clothianidin is classified as given in Tables 2-2:

Table 2-2 Proposed Classification based on Regulation (EC) No 1272/2008, Annex VI , Table 3.1 (ATP01, index number 613-307-00-5); the M-factor for chronic toxicity was added additionally)

	Classification	Wording
Hazard classes, Hazard categories	Acute Tox. 4 Aquatic acute 1 Aquatic chronic 1	
Hazard statements	H302	Harmful if swallowed
	H 400	Very toxic to aquatic life
	H410	Very toxic to aquatic life with long-lasting effects
M-Factors	Aquatic acute : 10 Aquatic chronic : 100	

The classification of the active substance implies the following precautionary statement for the environment: P273, P391, P501.

Classification and Labelling of SPU-02000-I-SC

Table 2-3 Proposed classification of SPU-02000-I-SC based on Directive 1999/45/EC

	Classification	Wording
Class of danger	Xi ; N	Irritating, Dangerous to the environment
R phrases	R43	May cause sensitisation by skin contact
	R50	Very toxic to aquatic organisms
	R53	May cause long-term adverse effects in the aquatic environment

Table 2-4 Proposed classification of SPU-02000-I-SC based on Regulation (EC) No 1272/2008

	Classification	Wording
Hazard classes, Hazard categories	Skin Sen. 1	

Hazard statements	H317	May cause an allergic skin reaction

Table 2-5 Proposed labelling of SPU-02000-I-SC based on Directive 1999/45/EC

Classification		Wording
Class of danger	Xi ; N	Irritating, Dangerous to the environment
R phrases	R43	May cause sensitisation by skin contact
	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 feeding stuffs
	S24	Avoid contact with skin
	S37	Wear suitable gloves
	S46	If swallowed, seek medical advice immediately and show this container or label

Table 2-6 Proposed labelling of SPU-02000-I-SC based on Regulation (EC) No 1272/2008

	Labelling	**Wording**
Pictograms	GHS07	
Signal Word	Warning	
Hazard statements	H317	May cause an allergic skin reaction
Precautionary statements	P102	Keep out of reach of children.
	P261	Avoid breathing spray
	P280	Wear protective gloves and protective clothing

	P333+P313	If skin irritation or rash occurs: Get medical advice/attention

Remark:

The product SPU-2000-I-SC contains a sensitising compound of concern. A lower limit concentration of this ingredient for classification as R43 is specified as 0.05% in Annex I of Directive 67/548/EC (29th ATP) and Regulation (EC) No 1272/2008. Therefore, the product SPU-2000-I-SC has to be classified and labelled according to Directives 67/548/EEC and 1999/45/EC as: Xi, R43, May cause sensitisation by skin contact and according to Regulation (EC) No 1272/2008 as: Skin Sens. Cat. 1, H317, May cause an allergic skin reaction.

Following the information of the applicant, the concentration of clothianidin in the biocidal product SPU-02000-I-SC is ≥ 2.5%. In respect of the environment the proposed classification and labelling of the active substance clothianidin has to be N, R 50-53.

In addition to clothianidin, the biocidal product contains a substance at a concentration > 0,1 % that has to be classified as N, R50. The threshold value for classification of a substance as "dangerous for the environment" is ≥ 0,1 % (see Directive 1999/45/EEC). All other ingredients of the biocidal product are not classified as hazardous for the environment.

Taking into consideration the lowest acute effect value for aquatic organisms (Chironomus riparius, EC50 = 0.029 mg/L, 48 h) and according to Directive 1999/45/EC (Annex III, part B, table 1b) the concentration of the active substance clothianidin in the biocidal product implies the classification as N "Dangerous to the environment", R50 "Very toxic to aquatic organisms" and R53 "May cause long-term adverse effects in the aquatic environment" (conventional method).

The following risk phrases regarding the environment are required for the insecticide SPU-02000-I-SC according to Directive 1999/45/EC:

Hazard symbol(s):	N	Dangerous to the environment
Risk phrases:	R50	Very toxic to aquatic organisms
	R53	May cause long-term adverse effects in the aquatic environment

Table 2-7 Proposed environmental classification of the biocidal product according to CLP regulation

Signal word:	Warning
Classification	Aquatic acute 1 Aquatic chronic 1
H-Statements	H 400: very toxic to aquatic life H410: very toxic to aquatic life with longlasting effects
M-Factors	Aquatic acute : 10 Aquatic chronic : 100

With the reference date of 1 June 2015 the following precautionary statement for the product is mandatory: P273, P391, P501.

2.2 Summary of the Risk Assessment

2.2.1 Human Health Risk Assessment

2.2.1.1 Effects assessment

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 < LD50 < 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. Neither dermal nor ocular irritation was 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.

Classification and Labelling for acute toxicity according to Directive 67/548/EEC:
Xn; R22

Classification and labelling for acute toxicity according to the Globally Harmonised System (GHS):

Acute Toxicity, hazard category 4; H302 (harmful if swallowed)

The active substance clothianidin is also included in Annex I of Dir. 91/414/EEC where diverging threshold values are set. The original threshold values for human health as derived by the Belgian authority during the pesticides evaluation and by Germany for the biocides evaluations (PT8 and PT18) did not differ.

In 2006, the Commission set differing AOEL (corresponding to AEL medium-term) and ARfD (corresponding to AEL acute) values under Directive 91/414/EEC.

The AOEL of 0.1 mg/kg bw/d as well as the ARfD of 0.1 mg/kg bw/d as set in Annex I of Directive 91/414/EEC are based on a very conservative evaluation of effects seen in pregnant dams in the developmental studies in rats (York, 1998a) and rabbits (York, 1998b), i.e. slightly reduced bodyweight gain and reduced feed intake between day 6 and 9 in rats (NOAEL/LOAEL: 10/40 mg/kg bw/d) and a slight increase in the incidence of clinical signs (scant faeces, orange urine) in the rabbit study (NOAEL/LOAEL: 10/25 mg/kg bw/d).

These values are not supported within the approval procedure as a biocidal active substance and after review of the data, which form the basis for this AOEL and ARfD, it is maintained that these threshold values should be based on the most relevant studies, with regard to nature and severity of the observed effects. An AOEL of 0.2 mg/kg bw/d (90-d dog study; NOAEL 20 mg/kg bw/d; AF 100) and an ARfD of 0.25 mg/kg bw/d (pharmacology study in mice, single administration of test compound, NOAEL of 25 mg/kg bw, AF 100) are considered adequate for human health risk assessment. This is in line with the AELs set for clothianidin during the evaluation of PT 8.

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 animal(s). 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 of 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.
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.

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. 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.

Pharmacological Study

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 LD50 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 tested positive in the bacterial reverse mutation test.

Medical Data

No medical reports on the manufacturing personnel have been submitted.

Biocidal Product

Acute toxicity and irritation studies result in no classification of the biocidal product SPU-02000-I-SC. The applicant did not submit a skin sensitisation study. Non-submission was accepted. Since the biocidal product contains a known sensitiser in considerable amounts it has to be classified/labelled as Xi, R43 (May cause sensitisation of the skin).

Summary and conclusion

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 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 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 results in a value of 0.1 mg/kg bw/d** (oral absorption > 90 %).
For clothianidin, it is not expected that residues in food or feeding stuffs will occur in relevant amounts for the applied uses. Anyhow, they cannot be excluded with certainty for further applications under PT 18. Therefore, based on the 2-year study in rats, supported by the 2-generation study in rats (NOAEL 10 mg/kg bw/d) an **ADI of 0.1 mg/kg bw/d** and based on a pharmacological study in mice (NOAEL 25 mg/kg bw) an **ARfD of 0.25 mg/kg bw** were derived.
A dermal absorption of 2 % was derived from a study in rhesus monkeys conducted with a similar product.
In the absence of data, inhalation absorption of 100 % is assumed.

2.2.1.2 Exposure assessment

Exposure of Professionals
Clothianidin is manufactured outside the EU and is imported as a solid. The formulation of the biocidal product SPU-02000-I-SC is performed in the chemical industry (EU). The exposure during the formulation of the biocidal product is not under the requirements of the BPD. However, it is assumed that the production is performed in conformity with national and European occupational safety and health regulations.
The biocidal product SPU-02000-I-SC is intended for use as an insecticide against flies in livestock and poultry stables by farmers (considered by the participant as professionals). The product may be used undiluted (2.6 % a.s., ready-to-use) by smearing (brushing) to small surface patches at the flies' preferred resting places using a brush or in diluted form (0.87 % a.s.) applied by spraying.
For the assessment of inhalation exposure, the main focus is set on exposure to dusts and to droplet aerosols, because, due to the low vapour pressure (vapour pressure of 3.8 x 10-11 Pa at 20°C), inhalation exposure to vapour is of minor pertinence.
The relevant scenarios for exposure assessment are:
Brushing application in animal housing,
Spraying application in animal housing and
Secondary exposure towards the biocidal product.
Potential exposure estimates concerning formulation and use of the representative biocidal product are performed not taking 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 % inhalation absorption (see table I 2-1 below). In all exposure scenarios skin contact significantly contributes to the total internal dose. The highest estimate results in an internal dose of 4.6 mg clothianidin/person/day for spraying (scenario 3).

During the brushing application, the potential inhalation exposure in the mixing & loading, application and post-application phase is assessed as negligible. Potential dermal exposure during mixing & loading is assessed as negligible as well, whereas during the application phase the estimated potential dermal exposure is 100.8 mg/person/day based on Model 3 (Consumer product painting) of the TNsG Human Exposure to Biocidal Products (Part 2, p. 202). For the calculation of the potential dermal exposure during the post-application phase, an approach of the CA of Finland during the assessment for Tolyfluanid was used, resulting in 17.7 mg/person/day. The total potential dermal exposure during the brushing application of SPU-02000-I-SC is 118.5 mg/person/day.

The spraying application assessment yielded in a potential inhalation exposure of 0.151 mg/m3 (shift average) for the application phase, potential inhalation exposure during mixing & loading and post-application phase is assessed as negligible. The potential dermal exposure during the mixing & loading phase was estimated with the Model Mixing & Loading (Europoem II database) TNsG Human Exposure to Biocidal Products (User Guidance, p. 25) resulting in 38.2 mg/person/day. During the application phase, the potential dermal exposure was assessed to be 190.0 mg/person/day, estimated based on Model 1 (Spraying) of the TNsG Human Exposure to Biocidal Products (Part 2, p. 143-145). The post-application dermal exposure is estimated with DEO unit 1 of the Riskofderm model (Riskofderm 2003, Warren et al. 2006) resulting in 2.4 mg/person/day. The total potential dermal exposure for all phases is 230.6 mg/person/day.

The secondary exposure of workers cannot be excluded. The inhalation exposure is assessed as negligible, whereas potential dermal exposure is estimated to be 72.4 mg/person/day with incidental contact.

Exposure of Non-Professionals
The biocidal product SPU-2000-I-SC is also used as an insecticide in households. The biocidal product is applied by brushing card boards with the paste. During application, dermal exposure may occur. Inhalation and oral exposure are unlikely. The biocidal product is applied in minimum once per year and in maximum over the summer season. Thus, acute and medium term primary exposure was estimated.
The exposure assessment yielded in an acute or medium-term exposure of 2.7 x 10-2 mg/kg bw(/d).
Secondary exposure to infants and adults is not expected if the biocidal product is used as intended according to manufacturer's instructions.

Risk characterisation

Risk characterisation for professionals
The exposure scenarios for clothianidin consist of two scenarios, the brushing and the spraying scenario, as well as the secondary exposure. For the potential exposure (without PPE) the risk characterisation for the brushing scenario and the secondary exposure is of no concern. For the spraying scenario, risk characterisation is of no concern only if appropriate protective measures are taken.
For risk characterisation, the total internal body burden resulting from the relevant exposure scenarios is compared to the AELlong-term of 0.1 mg/kg/d .
The AEL (as internal reference value) is based upon the oral long-term NOAEL of 9.7 mg/kg/d, a 10 x 10 assessment factor for inter- and intraspecies differences and on

results from toxicokinetics studies revealing a 100 % oral absorption. There are no relevant inhalation toxicity studies or dermal toxicity studies.
The risk characterisation for clothianidin, especially for the spraying scenario, is exclusively triggered by dermal contact. The actual dermal exposure estimate for clothianidin accounts for some kind of personal protective equipment to reduce potential dermal exposure.
Based on the exposure-to-AEL ratio of 0.9, the spraying scenario with the personal protective measures described (actual exposure) is not considered to result in unacceptable health risks (no concern).
The Human Health Tables for Risk Characterisation are represented in Appendix II.

Conclusion
The risk characterisation is considered to be sufficiently comprehensive and reliable for the purpose of the approval of clothianidin. It is essential to indicate, that the conclusion only apply to the active substance in the biocidal product (and not to other ingredients).

Safety Measures for Professionals
For spray-application, the estimated potential exposure leads to concern, predominantly via the skin. In order to keep the limit value, it is mandatory to wear adequate protective gloves during the 'mixing & loading'-phase of the spray-application, at least.
As stated before, occupational risks in the other scenarios evaluated are low regarding exclusively the active substance of the biocidal product. Nevertheless, it can be reasonable and necessary that the participant's dossier stipulates more detailed measures for handling the biocidal product than for the active substance due to further ingredients of the product, which are not taken into account here.

Risk Assessment for Non-Professionals
The primary exposure estimates are in all cases below the acute and the medium-term AEL (in maximum 14 % of AEL). All MOEs were above 740. Thus, it is concluded that primary exposure of non-professionals by the biocidal product is acceptable in relation to human health.
Secondary exposure to infants and adults is not expected if the biocidal product is used as intended according to manufacturer's instructions. It has to be clearly indicated in these instructions that cardboards or other objects, which have been treated with biocidal product, have to be kept out of the reach of children during use and after disposal. It is expected that improper application of the biocidal product may lead to considerable exposure levels, particularly for children.

Residues
Measurable residues in food or feed from the use of clothianidin in PT18 biocidal products are not expected. Therefore, an additional exposure to humans through diet arising from the use of clothianidin as a biocide can be excluded. No MRLs specific to biocidal product uses are necessary.
Crop use related MRLs for clothianidin in EU Member States have been defined according to Regulation (EC) No. 396/2005 and the proposed residue definition for food of plant and animal origin is "clothianidin" for risk assessment and monitoring.

Safety Measures for Non-Professionals
The biocidal product has to be labelled as given in 2.1.3. For non-professionals the product size should be restricted to 0.5 L and must be fitted with a child-safe fastening. The package size restriction is necessary based on the following two arguments:
The risk assessment for non-professional users is based on the assumption that a maximum of 0.05 L is used per application. However, no data on the actual usage amount are available. If more than 454 mL (approx. the package size restriction) are used at once, this would result in a non-acceptable human health risk.

The distribution of bigger packages would result in long-term storage in private households, which would significantly increase the risk for accidental exposure of infants and children.
The biocidal product is classified as R43 due to the presence of a co-formulant. According to the "Note for Guidance on authorisation of skin sensitiser biocidal products requiring PPE for non-professional users" (CA May14 doc 5.2a) biocidal products classified as skin sensitisers should, under normal circumstances, not be authorised for the non-professional user. In the event that biocidal products containing clothianidin in combination with sensitizing co-formulants at relevant concentrations are applied for at product authorisation, they must be evaluated according to the aforementioned note for guidance. If such products are subsequently authorised for non-professional use, either enclosure of suitable protective gloves into the packaging of the biocidal product or other appropriate risk mitigation measures can be taken into consideration. According to TNsG on human exposure (2007) it cannot be expected that non-professionals use any personal protection equipment, such as protective gloves, even if this is required on the label. However, if protective gloves are delivered within the biocidal product package use of them can be assumed. Depending on the potency of the sensistising co-formulant, the enclosure of suitable protective gloves in sufficient number by the applicant may be an appropriate measure to ensure safe handling of the biocidal product.

2.2.2 Environmental Risk Assessment

2.2.2.1 Fate and distribution in the environment

Biodegradation

Clothianidin is not readily biodegradable. In two German water-sediment systems partial degradation in biologically active systems was observed. However, primary degradation of clothianidin in the water phase and in the entire systems is slow (water: $DissT_{50}$: 58.4 and 94.4 days; entire system: $DegT_{50}$: 145.3 and 109.2 days converted to 12 ºC average EU outdoor temperature). 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. The metabolite TMG was observed in the sediments up to maximum levels of 21-23 % of applied radioactivity.
Degradation rate and route of clothianidin was investigated in veal calf, pig and chicken manure, respectively. The veal calf and pig manures were incubated under anaerobic laboratory conditions, the chicken manure samples under aerobic conditions. Despite aerobic incubation, anaerobic conditions prevailed within the chicken manure throughout the study. DT_{50} values of 25.4 – 59.9 days (at 12°C) were derived for clothianidin for the manures investigated. In the manure extracts, only the metabolite TMG was identified. The amount of TMG reached maxima of 55-58 % of the applied radioactivity. For the manures investigated, DT_{50} values of 259.2 – 375.5 days (at 12°C) were derived for TMG. The study results revealed that TMG is very persistent in manure and that TMG seems to be the main metabolite of the anaerobic degradation pathway of clothianidin.
From soil laboratory studies it can be concluded that clothianidin is persistent under aerobic conditions (geometric mean DT50 = 518 days at 20 ºC, corresponding to a DT50 of 983 days at 12 ºC). Mineralisation of clothianidin was found to be low to negligible (1.5 to 11.2 % after 120 days). 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 one soil. In the overall assessment of laboratory studies on aerobic biodegradation in soil, clothianidin is

categorised as persistent in soil. The DT50 values in soil at 20 ºC for the metabolites MNG are 82 to 108 days and 62 – 111 days for TZNG respectively. Converted to 12 ºC average EU outdoor temperature the half-lives amount to 156 – 205 days for MNG and 118 – 211days for TZNG.

The recalculation of DT50-values from eight European field studies due to FOCUS-kinetics results in a DT50 of 77.1 d and a DT_{90} of 1284.7 d at 12 °C (trigger endpoints, geometric mean values). The geometric mean value of the modelling endpoint used for PEC calculation is 429.8 d at 12 °C. These data confirm 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 degraded 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 resulted in an arithmetic mean K_{aOC} of 160 mL/g and an arithmetic mean K_{dOC} of 188 mL/g for clothianidin, respectively. Clothianidin was found to be stable during both processes, i.e. adsorption and desorption. The major soil metabolite MNG is characterised by a K_{aOC} of 21 mL/g whereas TZNG provided a K_{aOC} of 276 mL/g. The metabolites remained unchanged in the soil. 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. The majority of radioactivity was identified in the top soil samples and about 37 % - 55 % of applied radioactivity could not be recovered and was attributed to losses by mineralisation. Thus, under the given test design for agricultural soils a contamination of groundwater by clothianidin appears to be of less relevance.

Bioaccumulation

The low Pow indicates that clothianidin has low potential to bioaccumulate in organisms. Both estimated bioconcentration factors for the aquatic (BCFfish = 0.78) and the terrestrial compartment (BCFearthworm = 0.9) can be classified as low.

2.2.2.2 Effects assessment

Aquatic Compartment

Clothianidin is of low acute toxicity to fish (96h-LC50 > 100 mg/L) and only slightly toxic to daphnids (48h-EC50 = 26 mg/L[≠]) and green algae (96h-EbC50 = 55 mg/L; 96h-ErC50 > 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-EC10 = 0.4 µg/L). Also in a mesososm study freshwater insects were found to be highly affected by the substance (NOEC = 1 µg/L). A PNECwater of 0.08 µg/L was derived from the available studies by applying an assessment factor of 5 on the lowest effect value of 0.4 µg/L for Chironomus riparius.

In an activated sludge respiration inhibition test with sludge from domestic sewage treatment plant a NOEC of 1000 mg/L was found. A PNECmicroorganism of 100 mg/L was derived from the available study.

Sediment

Studies in which the test organisms were exposed to clothianidin via spiked sediment are not available. Therefore, the PNECsediment was derived from the PNECwater using the equilibrium partitioning method, resulting in a PNECsediment of 0.34 µg/kg ww.

Atmosphere

Clothianidin is not considered to be used as fumigant. The vapour pressure of clothianidin ranges from 3.8×10^{-11} to 1.3×10^{-10} Pa. Direct evaporation is not expected, consequently. The Henry's Constant is 2.9×10^{-11} at 20°C, therefore, clothianidin has a low potential of volatilizing from water. The half-life of clothianidin in the troposphere was estimated to be 2.8 hours (chemical lifetime: 4.1 hours) considering a global 24-hours mean OH-radical concentration. Based on these results, accumulation of clothianidin in the air is not to be expected.

Terrestrial Compartment

Tests with earthworms, carabid beetles, collembolan, plants and soil microorganisms have been provided by the applicant. The lowest effect value was the 77d-NOEC of 0.02 mg/kg dw obtained for Poecilus cupreus in a laboratory study. The $PNEC_{soil}$ is derived from the NOEC for *Poecils cupreus* using an assessment factor of 10 resulting in a $PNEC_{soil}$ of 2 µg/kg dw = 1.8 µg/kg ww.

The metabolite TMG is formed up to 50 % from degradation of clothianidin in manure and is released to the soil compartment via manure application. The only available effect value for TMG for the soil compartment is a soil microorganisms study according to OECD 216. At the only tested concentration of 0.21 mg/kg dw effects on nitrogen transformation were < 10 %. This is in the same range with effects found for clothianidin in a nitrogen transformation test. As no further effect data with terrestrial organisms are available for TMG and the metabolite is structurally related to the parent compound, it is assumed for the further assessment that the metabolite TMG has the same toxicity to soil organisms as the parent substance clothianidin. Therefore, the PNECsoil derived for clothianidin is also

[≠] *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.*

applicable for the assessment of the metabolite TMG in soil.

Clothianidin has shown to be highly toxic to bees both by oral and contact exposure. The 48-hour LD50 for oral toxicity was 0.0038 µg/bee. Currently, there is no assessment concept available how to derive a PNEC for bees. As clothianidin is a systemic insecticide, it is taken up from soil by plants and exposure to bees via nectar and pollen is possible. Therefore, as a first step, the effect value has to be recalculated into a concentration in pollen/nectar. The data from the oral exposure test can be transformed to mg a.s./kg nectar/pollen using the information given in the publication. There, it is stated that a dose of 0.016 µg a.s./bee is equivalent to 615 µg a.s./kg sucrose solution. From this it can be concluded that the LD50 of 0.0038 µg a.s./bee was equivalent to 146 µg a.s./kg sucrose = 146 µg a.s./kg nectar/pollen.

As a first approach, an assessment factor of 10 is applied to derive the $PNEC_{bee}$, resulting in a

$PNEC_{bee}$ of 14.6 µga.s./kg nectar/pollen.

2.2.2.3 PBT and vPvB assessment

P criterion: Half-life > 40 d freshwater or >120 d in freshwater sediment. > 120 d in soil

vP criterion: Half-life > 60 d freshwater or >180 d in freshwater sediment. > 180 d in soil

Studies of the dissipation of clothianidin in the water sediment system suggest for the whole system a DT_{50} of 109 and 145 days and a $DissT_{50}$ of 58 and 94 days for the water phase under aerobic conditions at an EU average outdoor temperature of 12°C. Since only two aerobic systems were examined the worst-case has to be assessed regarding the P and vP criteria. Although the $DissT_{50}$ cannot be used to conclude on the P criterion as it does not allow to differentiate between degradation and any other dissipation process, it supports the conclusion drawn from total system $DegT_{50}$ that the P and vP trigger values in freshwater are fulfilled under worst case consideration. Regarding the total system $DegT_{50}$ values, both P trigger values (freshwater and freshwater sediment) are fulfilled.

In laboratory studies on aerobic degradation in soil DT_{50}-values between 143 days and more than one year were measured at a temperature of 20°C (geometric mean = 518 days, n=9), corresponding to values from 271 days to >> 1 year at 12°C (geometric mean= 983 days, n=9). Taking into account the soil trigger values for the P and vP criteria of the REACH legislation, both trigger values are fulfilled for clothianidin.

Therefore, clothianidin can definitely be considered to fulfil the P criterion in freshwater/freshwater sediments as well as in soils. The vP criterion is fulfilled in freshwater and soil. The P and vP criteria are complied by clothianidin.

The metabolite TMG was observed in sediments of the aerobic water-sediment up to maximum levels of 23 % of applied radioactivity and in anaerobic manures (manure study) up to maximum levels of 58 % of applied radioactivity. TMG seems to be the main metabolite of the anaerobic degradation pathway of clothianidin. At least in anaerobic manure TMG is very persistent (DT_{50} 259.2 – 375.5 days at 12°C). No information is currently available about degradation half-lives in sediments.

B criterion: BCF > 2000, vB criterion: BCF > 5000

For Clothianidin the calculated bioconcentration factor in fish is 0.78 and for earthworm is 0.9. Therefore, neither the B- nor the vB-criterion is fulfilled.

T criterion: Chronic NOEC < 0.01 mg/L or CMR or endocrine disrupting effects

The EC_{10} (equivalent to NOEC) for chironomids, the most sensitive species, is 0.0004 mg/L after 28 days.

The T criterion is complied.

Even though the T-criterion as well as the P-, vP-criterion are fulfilled the active substance clothianidin is neither PBT- nor vP/vB - candidate as the B and vB-criteria are not fulfilled.

2.2.2.4 Exposure assessment

For environmental exposure estimation data about one representative biocidal product SPU-02000-I-SC is provided by the applicant. 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. The applicant's statement is deemed to be plausible during active substance evaluation.

For the life cycle stage "industrial/professional use" different environmental exposure assessments for the b.p. have been performed regarding the particular intended uses and applications. The b.p. is intended to be used solely indoors as an insecticide for the control of flies in livestock and poultry stables. Two application techniques are specified as (i) smearing / painting of the undiluted b.p. on patches, walls, piles, windowsills etc. using a brush, and (ii) low-pressure spraying of a dilute solution (0.5 L product in 1 L water) on surfaces specified under (i). In both cases, the standard packing size of 0.5 L b.p. is adequate for a stable of 200 m^2 floor area. This results in an application rate of 0.061 g m^{-2} per application.

A release of the b.p. via manure application is the main path of entry into the environment. A certain fraction of the insecticide used in animal housing (animal categories according to table 5.4 of the ESD) may be discharged with waste water to the STP.

The environmental exposures are assessed applying the EU Technical Guidance Document (TGD) on Risk Assessment (2003) and the OECD Emission Scenario Document Number 14 for Insecticides for Stables and Manure Storage Systems (OECD, 2006).

Predicted environmental concentrations (PECs) have been estimated for the terrestrial compartment including soil and groundwater and for the aquatic compartment including sewage treatment plant (STP), surface water, and sediment. The estimation of PECs is based on two emission models:

- Soil, due to manure applications carried out according to nitrogen immission standard from the Netherlands (170 kg N ha^{-1} yr^{-1}), afterwards to ground water and surface water and

- Waste water, which is subsequently treated by a sewage treatment plant, leading to releases to soil (via sludge deposition), surface water, sediment, and ground (pore) water.

The calculations of the releases of clothianidin during manure and slurry applications have been accomplished for all animal categories and subcategories according to OECD ESD No. 14. A detailed description for the emission scenario for insecticidal application in animal housings including also the input and output values is given in chapter IIB 8.3. For the soil compartment, the calculation of PEC assumes application of manure/slurry onto agricultural soils (arable land and grassland). Different approaches have been calculated:

- An unrealistic worst case situation without consideration of degradation of a.s. in soil;

- A more realistic situation, taking into account the degradation of a.s. in soil and carry over of a.s. residues due to successive manure application;

Concerning releases via manure to soil, the maximum PEC values in arable and grassland soil for nitrogen limited immission are associated with slurry application from veal calves (animal category: 3). For risk assessment with regard to the soil compartment, combined PEC values are derived from a.s. clothianidin and the relevant metabolite TMG, identified in the manure degradation study, as it is assumed that the metabolite TMG has the same toxicity to soil organisms as the active substance clothianidin. For both, PEC groundwater and PEC surface water (including sediment) estimation, a refinement step of the first approach (pore water calculation model and default dilution factor according to EU TGD (2003)) was accomplished using EU FOCUS scenarios based transport and fate simulation tools. The predicted concentrations in groundwater were significantly below the threshold criteria of 0.1 µg L^{-1} for all scenarios and for all soils (grassland and arable land). Release to surface water is also expected. Emission to air is negligible.

Particularly during the cleaning procedure of poultry housing systems, a fraction of the applied biocidal product can be released to waste water that is discharged to a STP. The species/categories taken to be under consideration are laying hens in battery cages (cat. 8) as well as laying hens in free range (cat. 11) and broilers in free range (cat. 12). The default release fractions to waste water given in the OECD-ESD were used for estimating the amount of clothianidin discharged to the STP.

2.2.2.5 Risk characterisation

Aquatic Compartment

For clothianidin, the applicant provided data for a representative product in different application areas and with different application rates. For the production and the formulation process no environmental exposure assessment and thus no risk characterisation was carried out. Within the scope of the product authorisation, it has to be checked again whether the production and formulation processes as described by the applicant still apply.

Two different emission pathways were identified regarding the aquatic compartment:

- Emission via manure application to soil leading to releases to surface water and sediment (indoor application in animal housings)

- Emission via wastewater to STP and subsequently to surface water and sediment (indoor application in animal housings, especially poultry stables)

Regarding the emission pathway via waste water to STP and subsequently to surface water and sediment, a risk for surface water and sediment was identified from the use of

clothianidin in poultry stables with a wastewater discharge to sewage treatment plants. It was concluded that a label restriction is necessary preventing the use of products containing clothianidin in animal housings where exposure to the STP or surface water is given. Consequently, direct releases from animal housings to surface water have to be avoided as well, unless it is clearly demonstrated at the stage of product authorisation that no risks to the environment will occur.

In summary, there is no risk for the aquatic compartment related to the use of clothianidin when implementing the necessary restriction for poultry stables as mentioned above.

Currently, no test about the elimination of clothianidin in sewage treatment plants (STP) is available. The environmental exposure assessment was performed without considering degradation in STP. Thus, the risk for surface water and sediment from the use of clothianidin containing products in poultry stables with a wastewater discharge to sewage treatment plants was identified as stated above. To refine the environmental exposure assessment, i.e. to demonstrate a potential degradation of clothianidin in STP, it is suggested performing an aerobic sewage treatment plant simulation study (OECD 303 A) at the stag of product authorisation.

Terrestrial Compartment including Groundwater

Two different emission pathways were identified regarding the terrestrial compartment:

- Emission via manure application leading to releases to soil and subsequently, to groundwater (indoor application in animal housings)

- Emission via wastewater to STP leading to releases to soil via sewage sludge deposition and subsequently, to groundwater (indoor application in animal housings/ especially poultry stables)

The following table gives an overview on the numbers of identified risks from product application by smearing and low pressure application for the soil compartment (arable land, grassland) considering the parent and the main metabolite TMG.

Table 2-8 Numbers of identified risks for the soil compartment after applying manure/slurry to arable land and grassland considering the full set of animal (sub-) categories

	Smearing application		Low-pressure spraying	
	Arable land	Grassland	Arable land	Grassland
Clothianidin: Number of animal (sub-)categories with risk in soil (total number of animal (sub-) categories)				
Cattle housings	0 (5)	2 (5)	0 (5)	3 (5)
Piggeries	0 (3)	3 (3)	0 (3)	3 (3)
Poultry housings	0 (12)	3 (12)	0 (12)	6 (12)
Metabolite TMG: Number of animal (sub-) categories with risk in soil (total number of animal (sub) categories)				
Cattle housings	0 (5)	2 (5)	0 (5)	3 (5)

Piggeries	0 (3)	3 (3)	0 (3)	3 (3)
Poultry housings	0 (12)	3 (12)	0 (12)	6 (12)
Clothianidin + TMG: Number of animal (sub-) categories with risk in soil (total number of animal (sub-) categories)				
Cattle housings	2 (5)	4 (5)	2 (5)	4 (5)
Piggeries	1 (3)	3 (3)	3 (3)	3 (3)
Poultry housings	0 (12)	7 (12)	0 (12)	11 (12)

In conclusion, no risks are identified in arable land for a.s. clothianidin for both application techniques. This is also valid for the metabolite TMG. Applying manure/slurry on grassland, risks are identified in all main animal categories (i.e. risks in several animal (sub-) categories of cattle housings, piggeries and poultries) for the a.s. as well as for the metabolite. In summary, regarding the risk assessment for the a.s and the metabolite as independent from each other (first and second subheading in Table 2-8) no risks are identified for the animal (sub-) categories 2 (beef cattle), 7-10 (laying hens in battery), 12 (broilers - litter floor) and 14 (parent broilers free range - grating floor).

Furthermore, if the a.s. and the metabolite are assessed together, risks in grassland and arable land are identified regardless of the application technique of the b.p. In this case, a safe use of clothianidin after application of manure is only given for animal (sub-) category 2 (beef cattle) with a PEC/PNEC of 0.75 and animal (sub-) category 8 (laying hens battery - belt drying) with a PEC/PNEC of 0.86.

Tables 2-9 and 2-10 give an overview of the PEC/PNEC ratios (clothianidin + TMG) determined for the soil compartment after applying manure/slurry to arable land or grassland respectively, considering the full set of animal (sub-) categories (PNECsoil = 1.8 µg/kg).

Table 2-9 PEC/PNEC-values (clothianidin + TMG) for the soil compartment after applying manure/slurry to arable land considering the full set of animal (sub-) categories (PNECsoil = 1.8 µg/kg)

Animal (sub) category	Smearing application		Low-pressure spraying	
	PEC (mg/kg)	PEC/PNEC	PEC (mg/kg)	PEC/PNEC
01 – dairy cattle	7.90E-04	0.44	1.13E-03	0.63
02 - beef cattle	2.35E-04	0.13	3.36E-04	0.19
03 - veal calves	1.92E-03	1.07	2.75E-03	1.53
04 - sows individual	1.37E-03	0.76	1.95E-03	1.08
05 - sows in groups	1.73E-03	0.96	2.47E-03	1.37
06 - fattening pigs	1.13E-03	0.63	1.61E-03	0.90
07 - laying hens battery - no treatment	4.05E-04	0.23	5.78E-04	0.32

08 - laying hens battery - belt drying	3.23E-04	0.18	3.87E-04	0.22
09 - laying hens battery- deep pit, high rise	4.52E-04	0.25	6.45E-04	0.36
10 - laying hens battery - compact	4.52E-04	0.25	6.45E-04	0.36
11 - laying hens free range - litter floor	1.37E-03	0.76	1.64E-03	0.91
12 - broilers - litter floor	5.82E-04	0.32	6.98E-04	0.39
13 - laying hens free range - grating floor	8.50E-04	0.47	1.21E-03	0.67
14 - parent broilers free range - grating floor	4.28E-04	0.24	6.11E-04	0.34
15 - parent broilers in rearing free range - grating floor	9.28E-04	0.52	1.33E-03	0.74
16 - turkey - litter floor	1.13E-03	0.63	1.36E-03	0.75
17 - ducks - litter floor	1.19E-03	0.66	1.43E-03	0.80
18 - gees - litter floor	8.48E-04	0.47	1.02E-03	0.57
01b - dairy cattle grazing season	1.87E-03	1.04	2.76E-03	1.48
02b - beef cattle - grazing season	5.27E-04	0.29	7.52E-04	0.42

Table 2-10 PEC/PNEC-values (clothianidin + TMG) for the soil compartment after applying manure/slurry to grassland considering the full set of animal (sub-) categories (PNECsoil = 1.8 µg/kg)

Animal (sub) category	Smearing application		Low-pressure spraying	
	PEC (mg/kg)	PEC/PNEC	PEC (mg/kg)	PEC/PNEC
01 – dairy cattle	3.16E-03	1.76	4.51E-03	2.51
02 - beef cattle	9.40E-04	0.52	1.34E-03	0.75
03 - veal calves	7.69E-03	4.27	1.10E-02	6.10

04 - sows individual	5.47E-03	3.04	7.81E-03	4.34
05 - sows in groups	6.93E-03	3.85	9.90E-03	5.50
06 - fattening pigs	4.51E-03	2.51	6.45E-03	3.58
07 - laying hens battery - no treatment	1.62E-03	0.90	2.31E-03	1.28
08 - laying hens battery - belt drying	1.29E-03	0.72	1.55E-03	0.86
09 - laying hens battery- deep pit, high rise	1.81E-03	1.00	2.58E-03	1.43
10 - laying hens battery - compact	1.81E-03	1.00	2.58E-03	1.43
11 - laying hens free range - litter floor	5.47-03	3.04	6.56E-03	3.65
12 - broilers - litter floor	2.33E-03	1.29	2.79E-03	1.55
13 - laying hens free range - grating floor	3.40E-03	1.89	4.86E-03	2.70
14 - parent broilers free range - grating floor	1.71E-03	0.95	2.45E-03	1.36
15 - parent broilers in rearing free range - grating floor	3.71E-03	2.06	5.30E-03	2.95
16 - turkey - litter floor	4.52E-03	2.51	5.42E-03	3.01
17 - ducks - litter floor	4.77E-03	2.65	5.73E-03	3.18
18 - gees - litter floor	3.89E-03	1.88	4.07E-03	2.26
01b - dairy cattle grazing season	7.48E-03	4.16	1.07E-02	5.94
02b - beef cattle - grazing season	2.11E-03	1.17	3.01E-03	1.67

Following the results from FOCUS PEARL (v. 4.4.4) calculations the predicted concentrations in groundwater were below the threshold value of 0.1 µg L^{-1} for all scenarios, both for grassland and arable land situations. Therefore, no risk to groundwater

is identified for the use of clothianidin in animal housings.

Considering the prospective intended use for control of flies in domestic premises (e.g. product is coated on carrier material, disposal via domestic waste) it was concluded that due to the intended application practice laid down by the applicant the exposure to the environment is negligible. Therefore, no environmental risk characterisation for clothianidin as a "household insecticide" has been carried out.

As clothianidin is a systemic insecticide and it has been shown that it is highly toxic to bees, a risk assessment for bees was performed. As currently no harmonized scenario is available, the assessment was based on a comparison of the $PNEC_{bee}$ and the PEC_{soil}. As a worst-case approach, it was assumed that the concentration in nectar and pollen is equivalent to the concentration in soil, i.e. a 100% uptake of clothianidin from soil by plants and a 100% transfer in nectar and pollen occurs. For the assessment, the highest PEC_{soil} values for arable land and grassland was used. The PEC/PNEC values for bees are below one. Therefore, it can be concluded that manure application contaminated with clothianidin to arable land as well as grassland will pose no risk to bees exposed to clothianidin via nectar and pollen. However, as currently no agreed concept for the assessment of the risk to bees is available, at product authorisation a revised risk assessment for bees might be necessary using the agreed assessment concept if available.

2.2.3 Assessment of endocrine disruptor properties

No specific test for potential endocrine disruption was carried out. However, from the available CMR studies and the repeated dose studies there is no evidence for endocrine disruption or for CMR effects.

2.3 Overall conclusion

The outcome of the assessment for clothianidin in product-type 18 is specified in the BPC opinion following discussions at the 7th meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA website.

2.4 List of endpoints

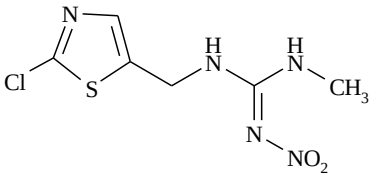
The most important endpoints, as identified during the evaluation process, are listed in Appendix I.

Appendix I: List of endpoints

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

Active substance (ISO Common Name)	Clothianidin
Product-type	18

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
CIPAC No	738
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)	930 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)	1.3×10^{-10} Pa (at 25°C) (extrapolated) 3.8×10^{-11} Pa (at 20°C) (extrapolated)
Henry's law constant (Pa m^3 mol^{-1})	2.9×10^{-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, buffered solution)
	pH_10_: 0.340 g/l (at 20 °C, buffered solution)
	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 clothianidin 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)
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)
Dissociation constant (additional data requirement from TNsG)	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 No absorption above 290 nm. No further absorption was detected.
Photostability (DT_{50}) (aqueous, sunlight source, 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
Flammability	Not highly flammable no relative self-ignition up to the melting point
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) Acute Tox. 4; H302 (Harmful if swallowed)
with regard to fate and behaviour data	**R 53** (May cause long-term adverse effects in the aquatic environment)
with regard to ecotoxicological data	**N; R 50** (Very toxic to aquatic organisms) Aquatic acute 1, H400 (very toxic to aquatic life) Aquatic chronic 1, H 410 (Very toxic to aquatic life with long-lasting effects)

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)	active substance and metabolites MNG and TZNG LC-MS/MS (ODS or Phenyl-hexyl column) LOQ = 0.005 mg/kg active substance HPLC-UV (RP-18 or CN column) LOQ= 0.01 mg/kg (not required)
Air (principle of method and LOQ)	active substance HPLC-UV (RP-18 or CN column) LOQ = 8 µg/m³
Water (principle of method and LOQ)	active substance in drinking and surface water: HPLC-UV (RP-18 or CN column) LOQ = 0.05 µg/L
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)	active substance HPLC-UV (RP-18 or CN column) LOQ = 0.01 mg/kg (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 > 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: 3-9 %, air: 0.017 %;

	limited enterohepatic circulation
Toxicologically significant metabolite	Parent compound 56-74%, TZNG and MNG ≥10%, MTCA ~8.5%, NTG ≤ 4% of applied dose + 9 further metabolites < 2% Livestock/plant/environmental metabolites more toxic than clothianidin, but occur at very low residue levels or are present in the rat, and thus toxicologically covered.

Acute toxicity

Rat (F 344) 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)

Repeated dose toxicity

Species/ target / critical effect	Haematopoetic organs (rat, dog)
Lowest relevant oral NOAEL / LOAEL	NO(A)EL: Dog: 650 ppm; 20 mg/kg bw/day (90 d WBC decrease; Rat: 500 ppm; 28 mg/kg bw/d (overall NOAEL; 90 d: RBC effects) Mouse: 500 ppm; 82 mg/kg bw/d (90 d: decreased bw gain, decreased food consumption) NOEL Mouse: 100 ppm; 16 mg/kg bw/d (90 d: mortality after ether narcosis; ether dose and duration of narcosis not specified)
Lowest relevant dermal NOAEL / LOAEL	NOAEL >1000 mg/kg bw (M+F) (28 d rat)
Lowest relevant inhalation NOAEL / LOAEL	No data, no study required

Genotoxicity	No genotoxic potential

Chronic Toxicity/Carcinogenicity

Target / critical effect	Interstitial ovarial gland hyperplasia, bw

	effects, feed consumption (2 yr rat)
Lowest relevant NOAEL / NOEL	NOAEL: 9.7 mg/kg bw/d
Carcinogenicity	No carcinogenic potential

Reproductive 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
Lowest relevant reproductive NOAEL / LOAEL	NOAEL <u>parental</u>: 31/37 mg/kg bw/d, (M/F) NOAEL <u>reproduction</u>: 31 mg/kg bw/d NOAEL <u>offspring</u>: 10 mg/kg bw/d
Species/Developmental target / critical effect	Rabbit: abnormalities of lung lobation, embryo lethality, decreased foetal weight, decreased ossification Rat: postnatal growth and development
Lowest relevant developmental NOAEL / LOAEL	NOAEL <u>maternal</u>: 25 mg/kg bw/d (rabbit) NOAEL <u>foetal</u>: 25 mg/kg bw/d (rabbit)

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	*Rat:* *Acute neurotoxicity NOAEL: 60 mg/kg bw/d (tremors, locomotor activity, hypothermia)* <u>Short-term</u> neurotoxicity NOAEL: 177 mg/kg bw/d <u>Developmental</u> neurotoxicity NOAEL: 43 mg/kg bw/d (startle habituation, motor activity)
Lowest relevant NOAEL / LOAEL.	43 mg/kg bw/d

Other toxicological 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
Pharmacological studies	Effects consistent with nicotinic CNS-

	stimulation and depression Mouse: decreased activity, increased hexobarbital-induced sleeping time, decreased intestinal transport, decreased hindlimb support Overall NOAEL : 25 mg/kg

Medical data

....	No data: new compound

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

* AEL: Systemic (= Internal) Acceptable Exposure Level

** Oral absorption

*** Not relevant for approval of clothianidin PT 18

Acceptable exposure scenarios (including method of calculation)
Professional users
Production of active substance: No evaluation. Clothianidin is produced outside the EU.

Formulation of biocidal product	No evaluation under the requirements of the BPD. OSH standards of the chemical industry are presumed.	
Intended use: spraying	Conc. biocidal product: 2.6 % a.s.(mixing and loading) and 0.87% a.s. (application and post-application)	
Mixing & loading: opening can, mixing and diluting b.p., loading sprayer, priming pump and spray line Model: TNsG Human Exposure Model 5 Spraying	Potential inhalation exposure (application)	0.151 mg/m^3
Application: Spray pressure: 1-3 bar, indoor use Form of exposure: aerosol during spraying Duration spraying: 80 min/d Frequency: once every 6 weeks, max. 5 times a year [1] No PPE Model: TNsG Human Exposure Model 1 Spraying Post-application: Unblock spray nozzle, cleaning Model post-application:RISKOFDERM DEO unit 1	Potential dermal exposure (all phases)	230.6 mg/person/day
Intended use: brushing	Conc. biocidal product 2.6 % a.s.	
Mixing and loading: opening can only (ready-to-use product)	Potential inhalation exposure (all phases)	negligible (expert judgement)
Application: Brushing in animal housing Duration: 160 min/d Frequency: once every 6 weeks, max. 5 times a year [1] No PPE Model: TNsG Human Exposure Model 3 Consumer Product Painting Post application: cleaning of the brush by rinsing and squeezing with cleaning rag Model: Exposure calculation based on an approach by the CA of Finland for	Potential dermal exposure (all phases)	118.5 mg/person/day

Tolylfluanid		
Secondary exposure	Working in animal housing	
Contact with active substance during typical work in animal housing Form of exposure: contact with treated wall surfaces or dust Duration: shift Frequency: incidental Model: expert judgement on the basis of 2.7 kg a.s. used for 1567 m^2 wall and roof area, palm of both hands (420 cm^2) could be exposed	Potential inhalation exposure	negligible
	Potential dermal exposure	72.4 mg/person/day
Non-professional users	Acute exposure acceptable Internal dose, adults, painting cards: 11% of $AEL\text{-}_{acute}$ Medium-term exposure acceptable Internal dose, adults, painting cards: 14% of $AEL\text{-}_{medium\text{-}term}$	
Indirect exposure as a result of use	Exposure not expected if applied as intended	

(1) It cannot be excluded that the product is used by professional pest control operators. In that case the frequency of use is estimated to be **3 times per week on a regular basis**, which would increase the concomitant exposure respectively.

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[2], TZMU[3], ACT•HCL[4] (formed only at elevated temperatures)
Photolytic 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[5], HMIO, FA, MU, CO_2. Modelled DT_{50} for the 50th degree of latitude: up to 23.4 d

[2] N-(2-chlorothiazol-5-ylmethyl)-N'-nitrourea
[3] N-(2-chlorothiazol-5-ylmethyl)-N'-methylurea
[4] 2-chlorothiazol-5-ylmethylamine hydrochloride
[5] methylguanidine

Quantum yield of direct phototransformation in water at Σ > 290 nm	0.014
Readily biodegradable (yes/no)	No
Biodegradation in seawater	Not relevant for intended use
Non-extractable residues	Aerobic: 27.6 – 43.3 % after 100 d Anaerobic: 80.9 % after 360 d
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) Water phase: $DT_{50\ persistence}$ (dissipation) = 30.8 and 49.8d Entire system: $DT_{50\ persistence}$ = 76.6. d and 57.6 d (recal.) converted to average EU outdoor temperature of 12°C: Water phase: $DT_{50\ persistence}$ (dissipation, 12°C) = 58.4 and 94.4d Entire system: $DT_{50\ persistence}$ (12°C) = 145.3 d and 109.2 d (recal.) 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) Water phase: DT_{50} (dissipation) = 4 d Entire system: DT_{50} = 21 d Converted to average EU outdoor temperature of 12°C: Water phase: DT_{50} (dissipation, 12°C) = 7.6 d Entire system: DT_{50} (12°C) = 40 d Mineralisation < 0.1 %
Distribution in water / sediment systems (metabolites)	Aerobic: Water: no metabolite detected Sediment: TMG[6] at max. level of 22.9 % (day 58)

[6] N-(2-chlorothiazol-5-ylmethyl)-N'-methylguanidine

	Anaerobic: Water: no metabolite detected Sediment: no metabolite > 5 %
Distribution in manure systems (active substance)	Anaerobic (veal calf, pig) and aerobic incubation (chicken, but this manure was anaerobic as well) at 20°C in the dark, 181 d max. 96-99 % AR (day 0); decline to not detectable (day 181) DT_{50} = 13.4 – 31.6 d (20°C, recal.) DT_{50} = 25.4 – 59.9 d (12°C, recal.) NER: max. 38 – 51 % AR Mineralisation: < 5 % AR after 181d
Distribution in manure systems (metabolites)	TMG: max. level of 55-58 % DT_{50} = 136.7-198.0 d (20°C, recal.) DT_{50} = 259.2 – 375.5 d (12°C, recal.) Other metabolites were only minor metabolites and were not identified.

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, geometric mean= 518 d, R^2 = 0.72 – 0.99) DT_{50lab} (converted to 12°C, aerobic): 271 d – >> 1 year (9 soils, geometric mean= 983 d)
	DT_{90lab} (20°C, aerobic): ---
	DT_{50lab} (10°C, aerobic): ---
	DT_{50lab} (20°C, anaerobic): ---
Field studies (state location, range or median with number of measurements)	Clothianidin: $DT_{50field,trigger}$ (12°C, geometric mean, n = 8, recalc.) = 77.1 d $DT_{90field,trigger}$ (12°C, geometric mean, n = 8, recalc.) = 1284.7 d $DT_{50field,modelling}$ (12°C, geometric mean, n = 8, recalc.) = 429.8 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

Non-extractable residues (Bound 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 a.i. (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 d

Adsorption/desorption

Parent compound:

Ka, Kd, Ka/Kd	Ka (n=5): 0.52 – 4.14 ml g^{-1} (arithmetic mean: 1.7 ml g^{-1}), 1/n: 0.81 – 0.87; Kd (n=5): 0.62 – 4.58 ml g^{-1} (arithmetic mean: 1.9 ml g^{-1}), 1/n: 0.81 – 0.88; Ka/Kd (n=5): 0.69 – 0.90;
Ka_{oc}, Kd_{oc}	Ka_{OC} (n=5): 84 – 345 ml g^{-1} (arithmetic mean: 160 ml g^{-1}); Kd_{OC} (n=5): 95 – 382 ml g^{-1} (arithmetic mean: 188 ml g^{-1})
pH dependence	No

Metabolites:

MNG:

Ka, Kd, Ka/Kd	Ka (n=5): 0.02 – 0.37 ml g^{-1} (arithmetic mean: 0.17 ml g^{-1}), 1/n: 0.70 – 1.10; Kd (n=3): 0.15 – 0.48 ml g^{-1} (arithmetic

	mean: 0.33 ml g^{-1}), 1/n: 0.88 – 0.97; Ka/Kd (n=3): 0.72 – 1.27;
Ka_{oc}, Kd_{oc}	Ka_{OC} (n=5): 5.2 – 34.3 ml g^{-1} (arithmetic mean: 21 ml g^{-1}); Kd_{OC} (n=3): 13.0 – 44.0 ml g^{-1} (arithmetic mean: 31 ml g^{-1})
TZNG:	
Ka, Kd, Ka/Kd	Ka (n=5): 0.63 – 4.71 ml g^{-1} (arithmetic mean: 2.3 ml g^{-1}), 1/n: 0.78 – 0.90; Kd (n=5): 0.83 – 5.75 ml g^{-1} (arithmetic mean: 2.7 ml g^{-1}), 1/n: 0.79 – 0.90; Ka/Kd (n=5): 0.76 – 0.88;
Ka_{oc}, Kd_{oc}	Ka_{OC} (n=5): 205 – 433 ml g^{-1} (arithmetic mean: 276 ml g^{-1}); Kd_{OC} (n=5): 271 – 527 ml g^{-1} (arithmetic mean: 340 ml g^{-1})

Mobility in soil

Lysimeter studies	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 a.s. 100 g in year 1 and 138 g in year 2, annual rainfall: 878 – 912 mm Lysimeter 2 and 3: grass, application of a.s. 160 g in yer 1 and 2, annual rainfall: 847 – 930 mm Leachates: a.s.: 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

Phototransformation 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)	n.a.
Surface water (indicate location and type of study)	n.a.
Ground water (indicate location and type of study)	n.a.
Air (indicate location and type of study)	n.a.

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 (based on nominal conc.) EC10 = 0.0004 mg/L (based on mean measured conc.)
Algae			
Selenastrum capricornutum	96 h	growth inhibition	E_bC_{50} = 55 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

* = in the evaluation of the same test after PPPD an EC50 of 40 mg/L was derived. However 70 % effect was reported at 32 mg/L test concentration. Therefore a recalculation of the EC50 value was performed resulting in an EC50 of 26 mg/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) = 0.2 mg/kg dwt soil * (mortality, reproduction)
Long-term toxicity to earthworms: field study (Annex IIIA, point XIII.3.2)	Natural earthworm population NOEC (1 year) = 0.15 mg/kg dw** (total number of earthworms/ total biomass/ number of individual species)
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 5 cm (used in the test system) and a soil density of 1500 kg/m³ for dry soil
**assuming a soil depth of 10 cm (default) and a soil density of 1500 kg/m³ for dry soil

Effects on soil micro-organisms

Nitrogen mineralization	< 25% effects at 0.1 mg and 0,5 mg a.s.* No significant effects after 28 days NOEC = 0.5 mg/kg dwt soil
Carbon mineralization	< 25% effects at 0.1 mg and 0,5 mg a.s.* No significant effects after 28 days 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

Effects on terrestrial vertebrates

Acute toxicity to mammals	Section A6.1
Short term toxicity to mammals	Section A6.3
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 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 (default) and a soil density of 1500 kg/m³ for dry soil

Effects on honeybees

Acute oral toxicity	LD50 (48 h) = 0.0038 µg/bee
Acute contact toxicity	LD50 (48 h) = 0.044 µg/bee

Effects on other beneficial arthropods

Poecilus cupreus (larvae)	NOEC (77d) = 0.02 mg/kg dw (mortality, development time and adult body weight) LC_{50} (77d) = 0.046 mg/kg dw

Bioconcentration

Bioconcentration factor (BCF)	BCF_{fish} = 0.78 (calc.) $BCF_{earthworm}$ = 0.9 (calc.)
Depuration time (DT_{50}) (DT_{90})	n.d.
Level of metabolites (%) in organisms accounting for > 10 % of residues	n.d.

Appendix II: List of Intended Uses

Object and/or situation (a)	Member State or Country	Product name	Organisms controlled (c)	Formulation		Application			Applied amount per treatment			Remarks (m)
				Type (d-f)	Conc. of a.s§ (i)	method kind (f-h)	number min max (k)	interval between applications (min)	g a.s./l min max		mg as/m^2 min max	
Fly control in stables and domestic premises ‡‡	EU	xxx	*Musca-spp (*flies)	SL (ready- to-use)	26g/L	painting,	Max 5 times during the fly season	6 weeks	26g/L ready-to-use formulation	500 mL / 200m² stable area	0.065 mg/m^2	
Fly control in stables	EU	xxx	*Musca-spp (*flies)		8g/L	spraying	Max 5 times during the fly season	6 weeks	8.7 g/L dilution	1500 mL/ 200m² stable area	0.065 mg/m^2	

‡‡ A biocidal product for consumer use (household insecticide) is not yet placed on the market. The prospective intended use is, however, described as follows: The product (paste formulation identical to Stallfliegenmittel Alba) will be coated onto a carrier material. A collecting pan for dead insects will be included in the product, enabling disposal of killed target insects via domestic waste. Releases of the a.i. and/or of the coating from the carrier material are not foreseen. Upon desiccation after a few weeks, the coating may be renewed by the user, as appropriate, using a disposable smearing tool added to the packaging. At the end of its service life, the product (i.e. carrier material including original and possibly supplemented coating) is foreseen to be disposed of via domestic waste.

Appendix III: Human Health Tables for Risk Characterisation

Table 1: Professional Users – Primary Exposure

Exposure Scenario (indicate duration)		Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg b.w/day] & Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
		estimated oral uptake [mg/kg b.w/day]	estimated inhalation uptake [mg/kg b.w/day] (1)	estimated dermal uptake [mg/kg b.w/day] (2)	estimated total uptake [mg/kg b.w/day]				
Application of biocidal product SPU-02000-I-SC									
Brushing (scenario 2)									
Tier 1 (no PPE)	Mixing&loading **ready-to-use paste (2.6 % active substance) once every 6 weeks, max. 5 times a year (3) :opening can only**		**-**	**-**	**-**	NOAEL= 9.7 mg/kg b.w./day		-	-
	Application ready-to-use paste (2.6 % active substance) once every 6 weeks, max. 5 times a year (3) :brushing in animal housing, 2.7 l biocidal product on average wall and roof area (1567 m^2), 160 min.		**-**	**0.03**	**0.03**	AEL long-term =0.1 mg/kg b.w./day	100	323	0.3
	Post-application ready-to-use paste (2.6 % active substance) once every 6 weeks, max. 5 times a year (3) :cleaning of the brush by rinsing and squeezing with cleaning rag		**-**	**0.006**	**0.006**			1616	0.06
	Total		**-**	**0.04**	**0.04**			242	0.4
Tier 2 (Refinement, PPE or other risk mitigation	Tier 2 is not required								

measures – Specify)									
Spraying (scenario 3)									
Tier 1 (no PPE)	**Mixing&loading** (2.6 % active substance) once every 6 weeks, max. 5 times a year [3] opening can + mixing and diluting product: 0.5 l biocidal product in 1 l water		-	0.01	0.01	NOAEL= 9.7 mg/kg b.w./day		970	0.1
	Application once every 6 weeks, max. 5 times a year [3] : (0.87 % active substance) low pressure spraying (1-3 bar) in animal housing:2.7 l biocidal product (undiluted equivalent) on average wall and roof area (1567 m^2), 80 min		**0.03**	0.06	0.09	AEL long-term =0.1 mg/kg b.w./day	100	108	0.9
	Post-application once every 6 weeks, max. 5 times a year [3] : (0.87 % active substance) unblock spray nozzle and cleaning, 5 min, no generation of splashes or aerosols		**-**	0.001	0.001			12125	0.008
	Total		**0.03**	0.08	0.11			88	1.1
Tier 2 (Refinement, PPE or other risk mitigation measures – Specify)	Mixing&loading		-	0.002	0.002			4850	0.02
	Application		0.03	0.06	0.09			108	0.9
	Post-application		-	0.001	0.001			12125	0.008
	Total		0.03	0.07	0.097			100	0.97

(1) 100 % inhalative absorption, breathing volume of 10 m^3 per shift

(2) 2 % systemic availability after dermal exposure

(3) It cannot be excluded that the product is used by professional pest control operators. In that case the frequency of use is estimated to be **3 times per week on a regular basis**, which would increase the concomitant exposure respectively

Table 2: Non Professional Users – Primary Exposure

Exposure Scenario (indicate duration)		Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg b.w./day] & Reference Value e.g.: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
		estimated oral uptake [mg/kg b.w./day]	estimated inhalation uptake [mg/kg b.w./day]	estimated dermal uptake [mg/kg b.w./day]	estimated total uptake [mg/kg b.w./day]				
Tier 1 (no PPE)	Application of SPU-2000-I-SC (acute or medium-term)	-	-	0.027	-	0.25 (AEL_{acute}) 0.20 ($AEL_{mid\text{-}term}$)	100 100	926 741	0.11 0.14
Tier 2 Refinement or other risk mitigation measures – Specify)	Not required								

Table 3: Indirect Exposure as a result of use - Secondary Exposure (non-professionals / bystander)

Exposure Scenario (indicate duration)		Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg b.w/day] & Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
		estimated oral uptake [mg/kg b.w/day]	estimated inhalation uptake [mg/kg b.w/day]	estimated dermal uptake [mg/kg b.w/day]	estimated total uptake [mg/kg b.w/day]				
Tier 1 (Worst case) Short Term Scenario	Not expected								
Exposure Scenario (indicate duration)		**Estimated Internal Exposure**				**Relevant NOAEL/ LOAEL [mg/kg b.w/day] & Reference Value e.g: AEL (acute or medium or chronic)**	**AF MOE_{ref}**	**MOE**	**Exposure /AEL**
		estimated oral uptake [mg/kg b.w/day]	**estimated inhalation uptake [mg/kg b.w/day]**	**estimated dermal uptake [mg/kg b.w/day]**	**estimated total uptake [mg/kg b.w/day]**				
Tier 2 (Refinement – Specify)	Not required								

Table 4: Indirect Exposure as a result of use - Secondary Exposure

Exposure Scenario (indicate duration)		Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg b.w/day] & Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
		estimated oral uptake [mg/kg b.w/day]	estimated inhalation uptake [mg/kg b.w/day]	estimated dermal uptake [mg/kg b.w/day]	estimated total uptake [mg/kg b.w/day]				
Tier 1 (Worst case) Chronic Scenario	Working in animal housing Incidental contact with active substance on wall surfaces during typical work in animal housing	-	-	0.02	0.02	NOAEL= 9.7 mg/kg b.w./day AEL long-term =0.1 mg/kg b.w./day	100	485	0.2
Exposure Scenario (indicate duration)		**Estimated Internal Exposure**				**Relevant NOAEL/ LOAEL [mg/kg b.w/day] & Reference Value e.g: AEL (acute or medium or chronic)**	**AF MOE_{ref}**	**MOE**	**Exposure /AEL**
		estimated oral uptake [mg/kg b.w/day]	**estimated inhalation uptake [mg/kg b.w/day]**	**estimated dermal uptake [mg/kg b.w/day]**	**estimated total uptake [mg/kg b.w/day]**				
Tier 2 (Refinement – Specify) Chronic Scenario	Not required								

Appendix IV – List of Terms and Abbreviations

Stand. term / Abbreviation	**Explanation**
% AR	Percent of applied radioactivity
ε	decadic molar extinction coefficient
≥	greater than or equal to
≤	less than or equal to
(Q)SAR	quantitative structure-activity relationship
<	less than
>	greater than
°C	degrees Celsius (centigrade)
µg	microgram
µL	microlitre
µm	micrometre (micron)
a	year
A/G	albumin/globulin ratio
ACh	acetylcholine
AChE	acetylcholinesterase
ACT•HCl	2-chlorothiazol-5-ylmethylamine hydrochloride
ADI	acceptable daily intake
ADME	administration distribution metabolism and excretion
AF	Assessment factors
ai	active ingredient
ALD_{50}	approximate median lethal dose, 50%
ALT	alanine aminotransferase (SGPT)
Ann.	Annex
ANOVA	analysis of variance
AOEL	acceptable operator exposure level
AOEL-S	Acceptable Operator Exposure Level short term

Stand. term / Abbreviation	**Explanation**
AP	alkaline phosphatase
approx	approximate
ARfD	acute reference dose
a.s.	active substance
AST	aspartate aminotransferase (SGOT)
ASV	air saturation value
AUC	Area under the curve
b.p.	biocidal product
BAF	bioaccumulation factor
BCF	bioconcentration factor
BOD	biological oxygen demand
bp	boiling point
BPD	Biocidal Products Directive
BUN	blood urea nitrogen
bw	body weight
c	centi- (x 10^{-2})
C&L	Classification and Labelling
CA	controlled atmosphere
CADDY	computer aided dossier and data supply (an electronic dossier interchange and archiving format)
CEC	cation exchange capacity
cf	confer, compare to
CFU	colony forming units
chap.	chapter
ChE	cholinesterase
CI	confidence interval
CL	confidence limits
cm	centimetre
Cmax	maximum concentration
CNS	central nervous system
CO2	Carbondioxid

Stand. term / Abbreviation	**Explanation**
COD	chemical oxygen demand
concentr.	concentration
CPK	creatinine phosphatase
CTNU	N-(2-chlorothiazol-5-ylmethyl)-N'-nitrourea
cv	coefficient of variation
d	day(s)
DIS	draft international standard *(ISO)*
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
dna	designated national authority
DO	dissolved oxygen
DOC	dissolved organic carbon
Doc.	document
dpi	days post inoculation
DRP	detailed review paper *(OECD)*
$DT_{50(lab)}$	period required for 50 percent dissipation (under laboratory conditions) (define method of estimation)
$DT_{90(field)}$	period required for 90 percent dissipation (under field conditions) (define method of estimation)
$DissT_{50}$	Dissipation half-life
$DegT_{50}$	Degradation half-life
dw	dry weight
DWQG	drinking water quality guidelines
e. g.	for example
EASE	Estimation and assessment of substance exposure
EC_{50}	median effective concentration
ECD	electron capture detector
ED_{50}	median effective dose

Stand. term / Abbreviation	**Explanation**
EDI	estimated daily intake
EINECS	European inventory of existing commercial substances
ELINCS	European list of notified chemical substances
ELISA	enzyme linked immunosorbent assay
e-mail	electronic mail
EMDI	estimated maximum daily intake
EN	European norm
EPMA	electron probe micro-analysis
ERL	extraneous residue limit
ESPE46/51	evaluation system for pesticides
EUSES	European Union system for the evaluation of substances
EWG	Europäische Wirtschaftsgemeinschaft
F_1	filial generation, first
F_2	filial generation, second
FA	formamide
FBS	full base set
FELS	fish early-life stage
FIA	fluorescence immuno-assay
FID	flame ionisation detector
$FLUX_{storage}$	Average daily flux i.e. the average quantity of an active ingredient (or any other substance of concern in a wood preservative product) that is daily leached out of 1 m² of treated wood during a certain storage period.
F_{mol}	fractional equivalent of the metabolite´s molecular weight compared to the active substance
FOB	functional observation

Stand. term / Abbreviation	**Explanation**
	battery
f_{oc}	organic carbon factor (compartment dependent)
fp	freezing point
FPD	flame photometric detector
FPLC	fast protein liquid chromatography
FS	flowable concentrate for seed treatment
g	gram(s)
GAP	good agricultural practice
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GEP	good experimental practice
GFP	good field practice
GGT	gamma glutamyl transferase
GI	gastro-intestinal
GIT	gastro-intestinal tract
GL	guideline level
GLC	gas liquid chromatography
GLP	good laboratory practice
GM	geometric mean
GOT	aspartate aminotransferase (SGOT)
GPC	gel-permeation chromatography
GPT	alanine aminotransferase (SGPT)
GSH	glutathione
H	Henry's Law constant (calculated as a unitless value)

Stand. term / Abbreviation	**Explanation**
h	hour(s)
ha	hectare(s)
Hb	haemoglobin
HC5	concentration which will be harmless to at least 95% of the species present with a given level of confidence (usually 95%)
Hct	haematocrit
HDT	highest dose tested
HEED	high energy electron diffraction
HID	helium ionisation detector
hL	hectolitre
HMIO	4-hydroxy-2-methylamino-2-imidazolin-5-one
HPAEC	high performance anion exchange chromatography
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography - mass spectrometry
HPPLC	high pressure planar liquid chromatography
HPTLC	high performance thin layer chromatography
HRGC	high resolution gas chromatography
H_S	Shannon-Weaver index
HSE	Health and safety Executive
Ht	haematocrit
I	indoor
I_{50}	inhibitory dose, 50%
IC_{50}	median immobilisation concentration or median inhibitory concentration 1
ICM	integrated crop management

Stand. term / Abbreviation	**Explanation**
ID	ionisation detector
IEDI	international estimated daily intake
IGR	insect growth regulator
im	intramuscular
inh	inhalation
INT	2-p-iodophenyl-3-p-nitrophenyl-5-phenyltetrazoliumchloride testing method
ip	intraperitoneal
IPM	integrated pest management
IR	infrared
ISBN	international standard book number
ISSN	international standard serial number
IUCLID	International Uniform Chemical Information Database
iv	intravenous
IVF	in vitro fertilisation
K	Kelvin
k	rate constant for biodegradation
k *(in combination)*	kilo
Ka	acid dissociation constant
K_{ads}	adsorption constant
Kb	base dissociation constant
K_{des}	apparent desorption coefficient
kg	kilogram
K_H	Henry´s Law constant (in atmosphere per cubic metre per mole)
K_{oc}	organic carbon adsorption coefficient

Stand. term / Abbreviation	**Explanation**
K_{om}	organic matter adsorption coefficient
K_{ow}	octanol-water partition coefficient
Kp	solid-water partition coefficient
kPa	kilopascal(s)
l, L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LCA	life cycle analysis
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LEV	Local exhaust ventilation
ln	natural logarithm
LOAEC	lowest observable adverse effect concentration
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOEC	lowest observable effect concentration
LOEL	lowest observable effect level
log	logarithm to the base 10
LOQ	limit of quantification (determination)
LPLC	low pressure liquid chromatography
LSC	liquid scintillation counting or counter
LSD	least squared denominator multiple range test
LSS	liquid scintillation spectrometry

Stand. term / Abbreviation	**Explanation**
LT	lethal threshold
m	metre
M	molar
MAC	maximum allowable concentration
MAK	maximum allowable concentration
max.	maximum
MC	moisture content
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MDL	method detection limit
MFO	mixed function oxidase
MG	methylguanidine
mg	milligram
MHC	moisture holding capacity
MIC	minimum inhibitory concentration
min	minute(s)
min	minutes
MKC	minimum killing concentration
mL, ml	millilitre
MLD	minimum lethal dose
MLT	median lethal time
mm	millimetre
MMAD	mass median aerodynamic diameter
MNG	N-Methyl-N'-nitroguanidine
mo	month(s)
MOE	margin of exposure
MOERef	Reference margin of exposure
mol	mole(s)
MOS	margin of safety

Stand. term / Abbreviation	**Explanation**
mp	melting point
MRE	maximum residue expected
MRL	maximum residue level or limit
MS	mass spectrometry
MSDS	material safety data sheet
msds	material safety data sheet
MT	material test
MTD	maximum tolerated dose
MU	methylurea
MW	molecular weight
n	number of observations
n-	normal (defining isomeric configuration)
n.a.	not applicable
NAEL	no adverse effect level
nd	not detected
NEDI	national estimated daily intake
NEL	no effect level
ng	nanogram
nm	nanometre
NMR	nuclear magnetic resonance
no, n°	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NPD	nitrogen-phosphorus detector or detection
NR, n.r.	not reported
NTE	neurotoxic target esterase
NTG	Nitroguanidine

Stand. term / Abbreviation	**Explanation**
OC	organic carbon content
OCR	optical character recognition
ODP	ozone-depleting potential
ODS	ozone-depleting substances
OEL	occupational exposure limit
OH	hydroxide
OJ	Official Journal
OM	organic matter content
OP's	operators
P	parental generation
Pa	pascal
PAD	pulsed amperometric detection
PAI	Purified active ingredient
PC	personal computer
PCV	haematocrit (packed corpuscular volume)
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_{GW}	predicted environmental concentration in ground water
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PED	plasma-emissions-detector
pH	pH-value
pKa	negative logarithm (to the base 10) of the acid dissociation constant
pKb	negative logarithm (to the base 10) of the base dissociation constant
PNEC	predicted no effect concentration (compartment to be added as subscript)

Stand. term / Abbreviation	**Explanation**
po	by mouth
ppb	parts per billion (10^{-9})
PPE	personal protective equipment
ppm	parts per million (10^{-6})
PPP	plant protection product
ppq	parts per quadrillion (10^{-24})
ppt	parts per trillion (10^{-12})
PRL	practical residue limit
PrT	prothrombin time
PT	product type
PTDI	provisional tolerable daily intake
PTT	partial thromboplastin time
PVC	Polyvinylchloride
$Q^*_{leach,time}$	Cumulative quantity of an active ingredient leached out of 1 m² of treated wood over a certain time period of service or storage prior to shipment, considered for assessment.
QA	quality assurance
QAU	quality assurance unit
$Q_{leach,storage,time}$	Cumulative quantity of an active ingredient in a wood preservative leached due to rainfall from treated wood stored, within a certain assessment period.
r	correlation coefficient
r^2	coefficient of determination
RA	risk assessment
RBC	red blood cell
RENI	Registry Nomenclature Information System
rev.	revision
Rf	retardation factor
RfD	reference dose
RH	relative humidity

Stand. term / Abbreviation	**Explanation**
RL_{50}	median residual lifetime
RMS	Rapporteur Member State
RNA	ribonucleic acid
RP	reversed phase
RPE	respiratory protection equipment
rpm	revolutions per minute
rRNA	ribosomal ribonucleic acid
RRT	relative retention time
RSD	relative standard deviation
s	second
S	solubility
S/L	short term to long term ratio
SAC	strong adsorption capacity
SAP	serum alkaline phosphatase
SAR	structure/activity relationship
SBLC	shallow bed liquid chromatography
sc	subcutaneous
sce	sister chromatid exchange
SCTER	smallest chronic toxicity exposure ratio (TER)
SD	standard deviation
sds	safety data sheet
se	standard error
SEM	standard error of the mean
SEP	standard evaluation procedure
SF	safety factor
SFC	supercritical fluid chromatography
SFE	supercritical fluid extraction
SIMS	secondary ion mass spectroscopy
SOP	standard operating procedures
sp	species (only after a generic

Stand. term / Abbreviation	**Explanation**
	name)
SPE	solid phase extraction
SPF	specific pathogen free
spp	subspecies
SSD	sulphur specific detector
SSMS	spark source mass spectrometry
STEL	short term exposure limit
STER	smallest toxicity exposure ratio (TER)
STMR	supervised trials median residue
STP	sewage treatment plant
t	tonne(s) (metric ton)
$t_{½}$	half-life (define method of estimation)
T_3	tri-iodothyroxine
T_4	thyroxine
TCD	thermal conductivity detector
TDR	time domain reflectrometry
TEP	typical end-use product
TER	toxicity exposure ratio
TER_I	toxicity exposure ratio for initial exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
tert	tertiary (in a chemical name)
TG	technical guideline, technical group
TGAI	Technical grade active ingredient
TGD	Technical guidance document
TGGE	temperature gradient gel electrophoresis

Stand. term / Abbreviation	**Explanation**
TID	thermionic detector, alkali flame detector
TIFF	tag image file format
TLC	thin layer chromatography
Tlm	median tolerance limit
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TMG	N-(2-chlorothiazol-5-ylmethyl)-N'-methylguanidine
TMRC	theoretical maximum residue contribution
TMRL	temporary maximum residue limit
TNsG	technical notes for guidance
TNsG	Technical Notes for Guidance
TOC	total organic carbon
TRGS	German Technical Rule for Hazardous Substances
tRNA	transfer ribonucleic acid
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
TZMU	N-(2-chlorothiazol-5-ylmethyl)-N'-methylurea
UDS	unscheduled DNA synthesis
UF	uncertainty factor (safety factor)
UV	ultraviolet
v/v	volume ratio (volume per volume)
vis	visible
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule to be applied after dispersion in water

Stand. term / Abbreviation	**Explanation**
wk	week(s)
WS	water dispersible powder for slurry seed treatment
wt	weight
ww	wet weight
XRFA	X-ray fluorescence analysis
yr	year(s)

Appendix V – List of Organisations

Abbreviation	**Explanation**
ASTM	American Society for Testing and Materials
BA	Biological Abstracts (Philadelphia)
BART	Beneficial Arthropod Registration Testing Group
BBA	German Federal Agency of Agriculture and Forestry
CA(S)	Chemical Abstracts (System)
CAB	Centre for Agriculture and Biosciences International
CAC	Codex Alimentarius Commission
CAS	Chemical Abstracts Service
CCFAC	Codex Committee on Food Additives and Contaminants
CCGP	Codex Committee on General Principles
CCPR	Codex Committee on Pesticide Residues
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Food
CE	Council of Europe
CEC	Commission of the European Communities
CEFIC	European Chemical Industry Council
CEN	European Committee for Normalisation
CEPE	European Committee for Paints and Inks
CIPAC	Collaborative International Pesticides Analytical Council Ltd
CMA	Chemicals Manufacturers Association
COREPER	Comite des Representants Permanents

Abbreviation	**Explanation**
COST	European Co-operation in the field of Scientific and Technical Research
DG	Directorate General
DIN	German Institute for Standardisation
EC	European Commission
ECB	European Chemicals Bureau
ECCO	European Commission Co-ordination
ECDIN	Environmental Chemicals Data and Information Network of the European Communities
ECDIS	European Environmental Chemicals Data and Information System
ECE	Economic Commission for Europe
ECETOC	European Chemical Industry Ecology and Toxicology Centre
EDEXIM	European Database on Export and Import of Dangerous Chemicals
EEC	European Economic Community
EHC	Environmental Health Criteria
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMIC	Environmental Mutagens Information Centre
EPA	Environmental Protection Agency
EPAS	European Producers of Antimicrobial Substances
EPFP	European Producers of

Abbreviation	**Explanation**
	Formulated Preservatives
EPO	European Patent Office
EPPO	European and Mediterranean Plant Protection Organization
ESCORT	European Standard Characteristics of Beneficials Regulatory Testing
EU	European Union
EUPHIDS	European Pesticide Hazard Information and Decision Support System
EUROPOEM	European Predictive Operator Exposure Model
EWMP	European Wood Preservation Manufacturers
FAO	Food and Agriculture Organization of the UN
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FRAC	Fungicide Resistance Action Committee
GATT	General Agreement on Tariffs and Trade
GAW	Global Atmosphere Watch
GIFAP	Groupement International des Associations Nationales de Fabricants de Produits Agrochimiques (now known as GCPF)
GCOS	Global Climate Observing System
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GEDD	Global Environmental Data Directory
GEMS	Global Environmental Monitoring System
GRIN	Germplasm Resources Information Network
IARC	International Agency for Research on Cancer

Abbreviation	**Explanation**
IATS	International Academy of Toxicological Science
ICBP	International Council for Bird Preservation
ICCA	International Council of Chemical Associations
ICES	International Council for the Exploration of the Seas
ILO	International Labour Organization
IMO	International Maritime Organisation
IOBC	International Organization for Biological Control of Noxious Animals and Plants
IPCS	International Programme on Chemical Safety
IRAC	Insecticide Resistance Action Committee
ISCO	International Soil Conservation Organization
ISO	International Organization for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JECFA FAO/WHO	Joint Expert Committee on Food Additives
JFCMP	Joint FAO/WHO Food and Animal Feed Contamination Monitoring Programme
JMP	Joint Meeting on Pesticides (WHO/FAO)
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
MITI	Ministry of International Trade and Industry, Japan
NATO	North Atlantic Treaty Organization
NAFTA	North American Free Trade

Abbreviation	**Explanation**
	Agreement
NCI	National Cancer Institute (USA)
NCTR	National Center for Toxicological Research (USA)
NGO	non-governmental organisation
NTP	National Toxicology Program (USA)
OECD	Organization for Economic Co-operation and Development
OLIS	On-line Information Service of OECD
OPPTS	Office of Prevention, Pesticides and Toxic Substances (US EPA)
OSPAR	Oslo Paris Convention (Convention for the Protection of the Marine Environment of the North-East Atlantic)
PAN	Pesticide Action Network
RIVM	Netherlands National Institute of Public Health and Environmental Protection
RNN	Re-registration Notification Network
RTECS	Registry of Toxic Effects of Chemical Substances (USA)

Abbreviation	**Explanation**
SETAC	Society of Environmental Toxicology and Chemistry
SI	Système International d'Unitès
SITC	Standard International Trade Classification
TOXLINE	Toxicology Information On-line
UBA	German Environmental Protection Agency
UN	United Nations
UNEP	United Nations Environment Programme
WFP	World Food Programme
WHO	World Health Organization
WPRS	West Palearctic Regional Section
WTO	World Trade Organization

Appendix VI – List of Studies

Data protection is claimed by the applicant in accordance with Article 60 of Regulation (EU) No 528/2012.

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
Doc IIIA					
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.	2000 a	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.	2000 b	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, 2000 non-GLP, unpublished	yes	SumiTake
A3.1.3/01*	Morrissey, M.A.; Kramer, H.T.	2000 a	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		

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
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.	2000 b	see A3.2/01		
A3.2/01	Morrissey, M.A.; Kramer, H.T.	2000 b	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.	2000 c	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

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
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, 2000 GLP, 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

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
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	yes	SumiTake

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			(TGAI). Covance, part of report no. 6155-119 SumiTake report no. DPCI019 March 1, 2001 non-GLP, unpublished		
A4.1/02* filed in confidential section	Kramer, H.T. Telleen, K.	2001 b	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.	2000 a	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 GLP, unpublished	yes	SumiTake / Bayer
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	yes	SumiTake / Bayer

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			SumiTake report no. DEFT034 November 30, 2000; 1st addendum March 13, 2001 GLP, unpublished		
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		1997a	TI-435: Acute oral toxicity study in the rat. report no. 586/120-1032 SumiTake report no. DTOX003 September 18, 1997 GLP, unpublished	yes	SumiTake
A6.1.1/02*		1997b	TI-435: Acute oral toxicity study in the mouse. report no. 586/121-1032 SumiTake report no. DTOX004 September 18, 1997 GLP, unpublished	yes	SumiTake

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A6.1.1/03*		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. report no. 108960-2; 97-912-OE December 30, 2002 GLP, unpublished Original report no. 108960; 97-412-OH;	yes	SumiTake
A6.1.2/01*		1997c	TI-435: Acute dermal toxicity study in the rat, report no. 586/122-1032 SumiTake report no. DTOX005 June 25, 1997 GLP, unpublished	yes	SumiTake
A6.1.3/01*		1998	TI-435: Single dose inhalation (head-only) toxicity study in the rat. report no. 586/129-D6154 SumiTake report no. DTOX014 April 21, 1998 GLP, unpublished	yes	SumiTake
A6.1.4/01*		1997d	TI-435: Skin irritation study in the rabbit. report no. 586/124-1032 SumiTake report no. DTOX006 June 25, 1997 GLP, unpublished	yes	SumiTake
A6.1.4/02*		1997e	TI-435: Eye irritation study in the rabbit. report no. 586/123-1032 SumiTake report no. DTOX007 July 30, 1997 GLP, unpublished	yes	SumiTake
A6.1.5/01*		1997	TI-435: Skin sensitisation study in the guinea pig. 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		2000c	TZNG: Acute oral toxicity study in the rat.	yes	SumiTake

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			report no. 586/163-D6144 SumiTake report no. DTOX025 January 20, 2000 GLP, unpublished		
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		1999c	TMG: Acute oral toxicity study in the rat. report no. 586/164-D6144 SumiTake report no. DTOX022 July 1999 GLP, unpublished	yes	SumiTake
A6.10.1/05		1999d	TMG: Reverse mutation in five histidine-requiring strains of *Salmonella typhimurium*. report no. 586/166-D5140 SumiTake report no. DTOX021 June 1999 GLP, unpublished	yes	SumiTake
A6.10.1/06		1999b	Methyl guanidine (MG): Acute oral toxicity study in the rat. report no. 586/153-D6144 SumiTake report no. DTOX017 February 1999 GLP, unpublished	yes	SumiTake
A6.10.1/07		1999c	Methyl guanidine: Reverse mutation in five histidine-requiring strains of Salmonella typhimurium report no. 586/151-D5140 SumiTake report no. DTOX019 February 1999 GLP, unpublished	yes	SumiTake
A6.10.1/08		1999c	TZMU: Acute oral toxicity study in the rat. report no. 586/152-D6144 SumiTake report no. DTOX016 February 1999 GLP, unpublished GLP, unpublished	yes	SumiTake
A6.10.1/09	Dawkes, N.	1999d	TZMU: Reverse mutation in five histidine-requiring strains of Salmonella typhimurium. Covance, England, report no. 586/150-D5140	yes	SumiTake

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			SumiTake report no. DTOX018 February 1999 GLP, unpublished		
A6.10.2/01*		2000	Pharmacological studies on TI-435. report no. 9L668 SumiTake report no. DTOX049 January 20, 2000 GLP, unpublished	yes	SumiTake
A6.2*		2000 d	[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*		2003	A study to determine the dermal absorption of TI 435 FS 600 when administered dermally to male Rhesus monkeys. report no. 200494 February 27, 2003 GLP, unpublished	yes	Bayer / SumiTake
A6.2/03	Yokota, T. et al. (2003), J Agric Food Chem 51, 7066-7072	2003	Yokota, T. et al. (2003). Absorption, tissue distribution, excretion, and metabolism of clothianidin in rats. J Agric Food Chem 51, 7066-7072	no	published
A6.3.1/01*		1997 a	TI-435: Toxicity to mice by dietary administration for 4 weeks. report no. TDA 180/960497 SumiTake report no. DTOX002 February 19, 1997 GLP, unpublished	yes	SumiTake
A6.3.1/02*		2000	4-week dietary toxicity study with TI-435 in dogs. report no. 6155-106 SumiTake report no. DTOX026 February 1, 2000 GLP, unpublished	yes	SumiTake
A6.3.1/03		1997 b	TI-435: Toxicity to rats by dietary administration for 4 weeks. report TDA 179/960496 SumiTake report no. DTOX001 February 19, 1997 GLP, unpublished	yes	SumiTake
A6.3.1/04		1998	Palatability pilot study for dietary concentrations of TI-435 in dogs. report no. 6155-107 SumiTake report no. DTOX015	yes	SumiTake

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			May 1, 1998 non-GLP, unpublished		
A6.3.2/01*		2000	28-day dermal toxicity study with TI-435 in rats. report no. 6155-120 SumiTake report no. DTOX060 October 13, 2000 GLP, unpublished	yes	SumiTake
A6.4.1/01*		2000a	13-week dietary toxicity study with TI 435 in dogs. report no. 6155-111 SumiTake report no. DTOX033 March 14, 2000 GLP, unpublished	yes	SumiTake
A6.4.1/02		2000b	52-week dietary chronic toxicity study with TI-435 in dogs. report no. 6155-113 SumiTake report no. DTOX034 March 22, 2000 GLP, unpublished	yes	SumiTake
A6.4.1/03*		2000	Technical grade TI 435: A subchronic toxicity testing study in the rat. report no. 109075 SumiTake report no. DTOX043; 98-172-QO February 22, 2000 GLP, unpublished	yes	SumiTake
A6.4.1/04		2000a	TI-435: Toxicity to rats by dietary administration for 13 weeks. Final draft report. report no. TDA 194/962814 SumiTake report no. DTOX052 September 8, 2000 non-GLP, unpublished	yes	SumiTake
A6.4.1/05*		2000b	TI-435: Toxicity to mice by dietary administration for 13 weeks. Final draft report. 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

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A6.6.1/02*	Otsuka, M.	1990 b	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.	1999 a	TI 453 : Salmonella/microsome test plate incorporation and preincubation method. First version of Bayer AG, report no. 28849, Revised version of Bayer AG, report no. 26584 SumiTake report no. DTOX041 June 16, 1999 GLP, unpublished	yes	SumiTake
A6.6.1/04*	Herbold, B.	1999 b	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*		2000 a	TI-435: L5178Y TK +/- mouse lymphoma assay. report no. 178/112 SumiTake report no. DTOX037 March 8, 2000 GLP, unpublished + Amendment 20.09.2000	yes	SumiTake
A6.6.3/02*		1999 a	TI-435: Mutagenicity study for the detection of induced forward mutations in the V79-HPRT assay in vitro. report no. 28851 report no. 26437.	yes	SumiTake

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			SumiTake report no. DTOX039 June 16, 1999 GLP, unpublished		
A6.6.4/01*		2000 b	TI-435: Micronucleus test in the mouse. 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*		(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 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*		2000 a	104-week dietary combined chronic toxicity and carcinogenicity study with TI-435 in rats. Volume I to XVI report no. 6155-108 SumiTake report no. DTOX046 April 11, 2000 GLP, unpublished + Amendment 28.11.2000	yes	SumiTake
A6.7/02*		2000 b	78-week dietary carcinogenicity study with TI-435 in mice. Volume I to VIII 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*		1998 a	Oral (gavage) developmental toxicity study of TI-435 in rats. report no. 1120-001 SumiTake report no. DTOX009 April 14,1998 GLP, unpublished	yes	SumiTake
A6.8.1/02*		1998 b	Oral (stomach tube) developmental toxicity study of TI-435 in rabbits. report no. 1120-002 SumiTake report no. DTOX013	yes	SumiTake

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			April 16,1998 GLP, unpublished		
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*		2000	A two generation reproductive toxicity study with TI-435 in the Sprague-Dawley rat. 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*		2000	An acute oral neurotoxicity screening study with technical grade TI-435 in Fischer 344 rats. report no. 108960 SumiTake report no. DTOX057; 97-412-OH, October 12, 2000 GLP, unpublished	yes	SumiTake
A6.9/02*		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 oral neurotoxicity screening study with technical grade TI-435 in Fischer 344 rats. SumiTake report no. DTOX059 report no. 108960-1; October 12, 2000 (original), November 8, 2000 (supplemental study); 00-N12-BA; 99-N12-BA GLP, unpublished	yes	SumiTake

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A6.9/03*		2000	A subchronic neurotoxicity screening study with technical grade TI-435 in Fischer 344 rats. SumiTake report no. DTOX058 report no. 109400; 97-472-OM October 12, 2000 GLP, unpublished	yes	SumiTake
A6.9/04*		2000	Developmental neurotoxicity study of TI-435 administered orally via the diet to Crl:CD BR VAF/Plus presumed pregnant rats. 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-D2142SumiTake report no. DEFT012June 5, 2000GLP, 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-248/00SumiTake report no. DEFT023September 19, 2000GLP, 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-121/00SumiTake report no. DEFT015April 19, 2000GLP, 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. DEFT031December 7, 2000GLP, 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-204/00SumiTake report no. DEFT009April 14, 2000GLP, unpublished	yes	SumiTake

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
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. DEFT005August 2, 1999GLP, 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-D2145SumiTake report no. DEFT004December 1999GLP, unpublished	yes	SumiTake
A7.1.2.1.2	Lewis, C.J.	2013	Degradation of [^{14}C]-Clothianidin in Veal Calf, Pig and Chicken Manure, Smithers Viscient (ESG) Ltd, UK, Study number: 3200029, unpublished	yes	Sumitomo Chemical Co. Ltd
A7.1.2.2.2/01 A 7.1.2.2.2/02	Gilges, M.; Brumhard, B. Reddemann, J.	2000 2000	see A7.1.2/01 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. DEFT011April 14, 2000Amendment no. 1 of April 14, 2001GLP, 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. DEFT032December 13, 2000Amendment no. 1 of April 9, 2001GLP, unpublished	yes	SumiTake
A7.1.3/01*	Lewis, C.J.	2000b	[^{14}C]TI-435: Adsorption/desorption in soil. Covance, report no. 586/139-D2142SumiTake report no. DEFT013August 17, 2000GLP, 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-518/00SumiTake report no. DEFT035January 17, 2001GLP, unpublished	yes	SumiTake

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A7.2.1/01*	Gilges, M.	2000	Aerobic degradation and metabolism of TI-435 in four soils. Bayer AG, report no. MR-497/99SumiTake report no. DEFT010March 13, 2000Amendment no. 1 of April 9, 2001GLP, 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-419/99SumiTake report no. DEFT014July 31, 2000Amendment no. 1 of April 9, 2001GLP, 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-2065/98SumiTake report no. DEFT018October 20, 2000GLP, 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-2066/98SumiTake report no. DEFT019October 20, 2000GLP, 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-2067/98SumiTake report no. DEFT020October 20, 2000GLP, 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-414/00SumiTake report no. DEFT021September 20, 2000GLP, 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-477/01SumiTake report no. DEFT041November 5, 2001GLP, unpublished	yes	SumiTake /Bayer

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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. TAK06SumiTake report no. DEFT029December 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. TAK05SumiTake report no. DEFT028December 19, 2000	yes	SumiTake
A7.2.2.4/03	Hellpointner, E.	1999 b	Photolysis of [Guanidine-^{14}C]TI-435 on soil surface.Bayer AG, report no. MR-154/99SumiTake report no. DEFT006August 30, 1999GLP, unpublished	yes	SumiTake
A7.2.3.1/01	Dorn, R.;Hein, W.	2000 a	Adsorption/desorption of ^{14}C-MNG, a degradate of TI-435, on five different soils.SLFA Neustadt, report of study no. TAK02SumiTake report no. DEFT025December 19, 2000GLP, 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. TAK01SumiTake report no. DEFT024December 19, 2000GLP, unpublished	yes	SumiTake
A7.2.3.1/03	Dorn, R.;Hein, W.	2000 b	Adsorption/desorption of ^{14}C-TZMU, a degradate of TI-435, on five different soils.SLFA Neustadt, report of study no. TAK03SumiTake report no. DEFT026December 19, 2000GLP, unpublished	yes	SumiTake
A7.2.3.1/04	Dorn, R.;Hein, W.	2000 c	Adsorption/desorption of ^{14}C-TMG, a degradate of TI-435, on five different soils.SLFA Neustadt, report of study no. TAK04SumiTake report no. DEFT027December 19, 2000GLP, unpublished	yes	SumiTake

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A7.2.3.2/01 *	Stupp, H.P.	2001 b	Degradation and translocation behavior of the insecticide active ingredient TI-435 under field conditions in a lysimeter (autumn application).Bayer AG, report no. MR-051/01SumiTake report no. DEFT037February 28, 2001GLP, unpublished	yes	SumiTake /Bayer
A7.2.3.2/02 *	Stupp, H.P.	2001 c	Degradation and translocation behavior of the insecticide TI-435 in a lysimeter under field conditions.Bayer AG, report no. MR-599/00SumiTake report no. DEFT036March 16, 2001GLP, 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-705/98SumiTake report no. DEFT008September 9, 1998non-GLP, unpublished	yes	SumiTake
A7.4.1.1/01 *		1998 a	TI-435 technical, fish (Rainbow trout), acute toxicity test, 96 h, limit test. no. 970714TA/FAR54472/CFF54472 SumiTake report no. DECO002January 6, 1998GLP, unpublished	yes	SumiTake
A7.4.1.1/02		2000 a	TI-435 technical: A 96-hour static acute toxicity test with the bluegill (Lepomis macrochirus, report no. 110003/149A-123SumiTake report no. DECO056October 27, 2000GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.1/03		2000	N-Methylnitroguanidine - Acute toxicity (96 hours) to Rainbow trout (Oncorhynchus mykiss) in a static test (limit test), report no. DOM 20038 SumiTake report no. DECO069October 5, 2000 GLP, unpublished	yes	SumiTake /Bayer
A7.4.1.1/04		2000 a	TI 435-Thiazolylnitroguanidine - Acute toxicity (96 hours) to Rainbow trout (Oncorhynchus mykiss) in a static test (limit test), report no. DOM 20039 SumiTake report no. DECO070September 14, 2000GLP, unpublished	yes	SumiTake /Bayer

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A7.4.1.1/05		2000b	TI 435-thiazolylmethylguanidine – Acute toxicity (96 hours) to Rainbow trout (Oncorhynchus mykiss) in a static test (limit test). Version 3, report no. DOM 20040 SumiTake report no. DECO068September 14, 2000GLP, 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-122SumiTake report no. DECO057Date: October 27, 2000GLP, 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. 970714TASumiTake report no. DECO001December 15, 1997, amended December 15, 2000GLP, 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 232SumiTake report no. DECO072September 22, 2000GLP, 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 231SumiTake report no. DECO073September 22, 2000GLP, 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 229SumiTake report no. DECO071September 22, 2000GLP, 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-102SumiTake report no. DECO051October 27, 2000GLP, unpublished	yes	SumiTake

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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/CSO54471SumiTake report no. DECO004January 6, 1998GLP, 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 20035SumiTake report no. DECO075September 27, 2000GLP, 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 20036SumiTake report no. DECO076October 5, 2000GLP, 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 20037SumiTake report no. DECO074September 29, 2000GLP, 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-D2145SumiTake report no. DECO045June 30, 2000GLP, unpublished	yes	SumiTake
A7.4.3.2/01 *		2000	TI-435 Technical: An early life-stage toxicity test with the fathead minnow (Pimephales promelas), report no.110163/149A-124B SumiTake report no. DECO059Date: December 13, 2000GLP, 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/CDR54471SumiTake report no. DECO010June 4, 1998GLP, unpublished	yes	SumiTake

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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. DECO018April 30, 1999GLP, 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. DECO014December 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-D2145SumiTake report no. DECO064January 9, 2001GLP, 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-125SumiTake report no. DECO058October 30, 2000GLP, 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. DECO082March 14, 2001GLP, 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. 17938SumiTake report no. DECO 030December 7, 1999GLP, 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/213200SumiTake report no. DECO079October 16, 2000GLP, unpublished	yes	SumiTake /Bayer

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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/213100SumiTake report no. DECO078October 16, 2000GLP, 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/213000SumiTake report no. DECO077October 16, 2000GLP, 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. DECO005February 23, 1998GLP, 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. 991207BKSumiTake report no. DECO083October 25, 2000GLP, 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. RRA66531SumiTake report no. DECO050October 23, 2000GLP, 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. RRA66521SumiTake report no. DECO049October 23, 2000GLP, 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. P3CRSumiTake report no. DECO084February 6, 2001GLP, unpublished	yes	SumiTake /Bayer

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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. P4CRSumiTake report no. DECO085February 6, 2001GLP, 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. 197-126SumiTake report no. DECO052October 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. 197-127SumiTake, report no. DECO053October 26, 2000GLP, 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-NREfSumiTake report no. DECO034October 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		
A 7.5.2.1/05	Womack, J.G., Mills, H.	2000	Field study to determine the effects of TI-435 50% WDG on earthworms. Covance Laboratories Ltd., Harrogate, North Yorkshire, England; report no. 586/198-D2143, GLP2000, unpublished		

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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		1998a	TI-435 technical acute oral toxicity (LD_{50}) to Bobwhite quail, report no. TDA 232/973538 SumiTake report no. DECO008June 1, 1998GLP, unpublished	yes	SumiTake
A7.5.3.1.1/02		1999	TI-435 technical: An acute oral toxicity study with the Japanese quail, report no. 197-128 SumiTake report no. DECO033January 6, 2000GLP, unpublished	yes	SumiTake
A7.5.3.1.2/01		1998b	TI-435 technical: Dietary LC_{50} to the Bobwhite quail, report no. TDA 233/973539 SumiTake report no. DECO007March 20, 1998GLP, unpublished	yes	SumiTake
A7.5.3.1.2/02		1998c	TI-435 technical: Dietary LC_{50} to the Mallard duck, report no. TDA 234/973540 SumiTake report no. DECO009June 1, 1998GLP, unpublished	yes	SumiTake
A7.5.3.1.3/01		2000a	TI-435 technical: A reproduction study with the Northern Bobwhite (Colinus virginianus), report no. 197-122 SumiTake report no. DECO031January 17, 2000GLP, unpublished	yes	SumiTake
A7.5.3.1.3/02		2000b	TI-435 technical: A reproduction study with the Mallard (Anas platyrhynchos), report no. 197-123 SumiTake report no. DECO032January 17, 2000GLP, unpublished	yes	SumiTake
A 7.5.4.1/01	Neumann, P.	2000	Acute effects of TI-435 (techn.) on larvae of carabid beetles *(Poecilus cupreus)* under extended laboratory test conditions. Bayer AG, 51368 Leverkusen-Bayerwerk, Germany; report no. NNP/PC018, 2000GLP, unpublished		

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A8/01	DE	1999	Allgemeine Verwaltungsvorschrift zum Wasserhaushaltsgesetz über die Einstufung wassergefährdender Stoffe in Wassergefährdungsklassen (Verwaltungsvorschrift wassergefährdende Stoffe – VwVwS)		Published
A8/02	EU	2001	European Waste Catalogue Commission Decision 2001/573/EC of 23 July 2001		Published
A9/01	EU		Directive 67/548/EEC on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances		Published

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Doc IIIB					
B3.1.1/01	Warncke, U.	2005	Determination of the physical-chemical properties of the test item SPU-02000-I Spiess-Urania Chemicals GmbH, Christinenthal, Germany, Report No.: U05PCI02 GLP, Not Published	Y	SPU
B4.1/01	Lüdke, S.	2005	Validated method of analysis for the determination of Clothianidin in xxx (SPU-02000-I) Spiess-Urania Chemicals GmbH, Christinenthal, Germany, Report No.: Wa-26-04-05-Alba GLP, Not Published	Y	SPU
B5.10.2/01	Saggau, B.	2006	Evaluation of the long term effect of xxx against stable fly (Musca autumnalis) (Stallfliege) (MUSCAU) and house fly (Musca domestica) (MUSCDO) "Spraying application" Spiess-Urania Chemicals GmbH, Christinenthal, Germany, Report No.: I05101 GLP, Not Published	Y	SPU

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Doc IIIB					
B5.10.2/02	Saggau, B.	2006	Evaluation of the long term effect of xxx against stable fly (Musca autumnalis) (Stallfliege) (MUSCAU) and house fly (Musca domestica) (MUSCDO) "Painting application" Spiess-Urania Chemicals GmbH, Christinenthal, Germany, Report No.: I05103 GLP, Not Published	Y	SPU
B5.10.2/03	Saggau, B.	2006	Evaluation of the dose response relationship of xxx against stable fly (Musca autumnalis) (Stallfliege) (MUSCAU) and house fly (Musca domestica) (MUSCDO) "Spraying application" Spiess-Urania Chemicals GmbH, Christinenthal, Germany, Report No.: I05102 GLP, Not Published	Y	SPU
B5.10.2/04	Saggau, B.	2006	Evaluation of the dose response relationship of xxx against stable fly (Musca autumnalis) (Stallfliege) (MUSCAU) and house fly (Musca domestica) (MUSCDO) "Painting application" Spiess-Urania Chemicals GmbH, Christinenthal, Germany, Report No.: I05104 GLP, Not Published	Y	SPU
B5.10.2/05	Röhlig, U	2005	Efficacy evaluation of xxx on the house fly Musca domestica L. under laboratory conditions (paint-application) BioChem agrar, Gerichshain, Germany, Report No.: 05 10 48 506 GLP, Not Published	Y	SPU
B6.1.1/01	Chevalier, F.	2005	Acute oral toxicity study of SPU-02000-I in CD rats LPT, Hamburg, Germany, Report No.: 19412/05 GLP, Not Published	Y	SPU
B6.1.2/01	Chevalier, F.	2005	Acute dermal toxicity study of SPU-02000-I in CD rats LPT, Hamburg, Germany, Report No.: 19413/05 GLP, Not Published	Y	SPU

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Doc IIIB					
B6.2/01	Leuschner, J.	2005	Acute dermal irritation/corrosion test (patch test) of SPU-02000-I in rabbits LPT, Hamburg, Germany, Report No.: 19414/05 GLP, Not Published	Y	SPU
B6.2/02	Leuschner, J.	2005	Acute eye irritation/corrosion test (patch test) of SPU-02000-I in rabbits LPT, Hamburg, Germany, Report No.: 19415/05 GLP, Not Published	Y	SPU
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