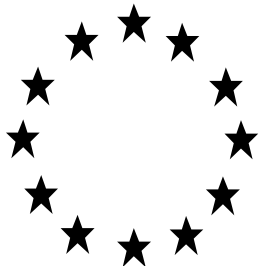
Directive 98/8/EC concerning the placing biocidal products on the market

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

Assessment Report



Tolylfluanid

Product-type 8
(Wood preservatives)

25 March 2009

Annex I - Finland

Tolylfluanid (PT 8)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 15 May 2009 in view of its non-inclusion in Annex I to Directive 98/8/EC

CONTENTS

STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

This assessment report has been established as a result of the evaluation of tolylfluanid as product-type 8 (wood preservatives), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with a view to the possible inclusion of this substance into Annex I or IA to the Directive.

Tolylfluanid (CAS no. 731-27-1) was notified as an existing active substance, by LANXESS Deutschland GmbH, hereafter referred to as the applicant, in product-type 8.

Commission Regulation (EC) No 2032/2003 of 4 November 2003[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive. (This Regulation has been repealed by Commission Regulation (EC) No 1451/2007 of 4 December 2007.)

In accordance with the provisions of Article 5(2) of that Regulation, Finland was designated as Rapporteur Member State (RMS) to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for tolylfluanid as an active substance in Product Type 8 was 28th March 2004, in accordance with Annex V of Regulation (EC) No 2032/2003.

On 26th March 2004, Finnish competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 24th September 2004.

On 13th April 2006, the Rapporteur Member State submitted, in accordance with the provisions of Article 10(5) and (7) of Regulation (EC) No 2032/2003, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 24th April 2006. The competent authority report included a recommendation for the inclusion of tolylfluanid in Annex I to the Directive for product-type 8.

In accordance with Article 12 of Regulation (EC) No 2032/2003, the Commission made the competent authority report publicly available by electronic means on 19th May 2006. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the

1 Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1

2 Commission Regulation (EC) No 2032/2003 of 4 December 2003 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, 24.11.2003, p. 1

Commission. Revisions agreed upon were presented at technical and competent authority meetings and the competent authority report was amended accordingly.

On 27th April and 16th May 2007, the RMS informed the Commission and other Member States (OMSs) about the new degradation product of tolylfluanid and the possible formation of N-nitrosodimethylamine (NDMA) during ozonation. The issue was discussed at the Technical Meeting (TMII07) and a new deadline for the revision of tolylfluanid wood preservative assessment and discussion was set to TMV07 in December 2007.

On 23rd November 2007, the RMS submitted a risk assessment of N,N-dimethylsulfamide (N,N-DMS) to the biocide technical meeting in December 2007. The first discussion on N,N-dimethylsulfamide risk assessment was focussed on groundwater risk of N,N-dimethylsulfamide calculated from tolylfluanid wood preservative use and proposed risk mitigation methods.

On 14th February 2008, the RMS submitted the toxicological part of the N,N-dimethylsulfamide risk assessment to the Commission and OMSs and the completed evaluation of the toxicological information was discussed at the Technical Meeting in March 2008 (TMI08).

On 22nd September 2008, the RMS submitted refined risk assessment of N,N-dimethylsulfamide and tolylfluanid draft assessment report to the Biocides Technical Meeting (TMIII08). It was concluded that tolylfluanid should be discussed at a CA Meeting.

On 27th November 2008 the draft assessment report of tolylfluanid was discussed for the first time at a Competent Authority Meeting (31st meeting). A revised version of the assessment report was discussed at the 32nd CA Meeting on February 2009.

On the basis of the final competent authority report, the Commission proposed the inclusion of tolylfluanid in Annex I to Directive 98/8/EC and consulted the Standing Committee on Biocidal Product on XX 2009.

In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on XX 2009.

1.2. Purpose of the assessment report

This assessment report has been developed and finalised in support of the decision to include tolylfluanid in Annex I to Directive 98/8/EC for product-type 8. The aim of the assessment report is to facilitate the authorisation in Member States of individual biocidal products in product-type 8 that contain tolylfluanid. In their evaluation, Member States shall apply the provisions of Directive 98/8/EC, in particular the provisions of Article 5 as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available at the Commission website[3], shall be taken into account.

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

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

The overall conclusion from the evaluation is that it may be expected that there are products containing tolylfluanid for the product-type 8, which will fulfil the requirements laid down in Article 5 of Directive 98/8/EC. This conclusion is however subject to:

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

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

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

Furthermore, these conclusions were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Article 5(1) and of the common principles laid down in Annex VI to Directive 98/8/EC.

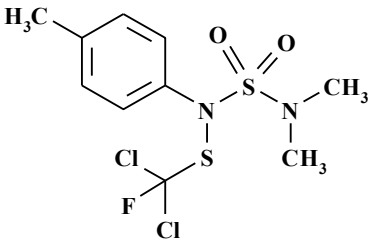
2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance and degradation products

2.1.1. Identity

CAS-No	731-27-1
EINECS-No.	211-986-9
Other No. (CIPAC, ELINCS)	CIPAC No. 275
IUPAC Name	N-(Dichlorofluoromethylthio)-N',N'-dimethyl-N-p-tolylsulfamide
C.A. Name	Methanesulfenamide, 1,1-dichloro-N-[(dimethylamino)sulfonyl]-1-fluoro-N-(4-methylphenyl)-

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

Common name, Synonyms	Tolylfluanid KUE 13183 B Preventol A5-S Euparen M Preventol A 5 Preventol VPOC 3017
Molecular formula	$C_{10}H_{13}Cl_2FN_2O_2S_2$
Structural formula	
SMILES	CN(C)S(=0)(=0)N(SC(F)(CL)CL)c1ccc(C)cc1
Molecular weight (g/mol)	347.3
Minimum purity	96% ww

Identification of the representative product

Trade name	Not applicable, because the product is a theoretical product (a Guide Recipe)		
Manufacturer´s development code number(s)	JJT 3580		
Ingredient of preparation	Function	Content	Classification of single components
Tolylfluanid	Active substance	0.7% w/w	See Chapter 2.1.6.
Naphtha (petroleum), hydrotreated heavy (white spirit)	Solvent	85.7% w/w	Xn, R65-66
Physical state of preparation	Liquid		

Nature of preparation Ready to use biocidal product

The full details of identity of the representative product are confidential and can be found in the Annex of Confidential Data and Information.

The active substance shall comply with the specification given in Chapter 1 of Appendix I of this report. The impurities are not expected to differ in toxicological significance from the parent compound, and the small differences in concentrations of the impurities in the different batches of tolylfluanid used for toxicity testing do not alter the validity of the current assessment of the health effects of tolylfluanid as technical active substance. Information on toxicity of impurities is included in the Confidential Annex.

The evaluation has established that for the active substance notified by Lanxess Deutschland GMBH, the rest of the manufacturing impurities considered are not, on the basis of information currently available, of toxicological or environmental concern.

The main degradation products are DMST (N,N-dimethyl-N'-p-tolylsulphamide) and N,N-dimethylsulfamide, which both have been taken into account and evaluated in the risk assessment.

2.1.2. Physico-Chemical Properties

Tolylfluanid is a solid substance (colourless crystalline powder, technical active ingredient, or colourless crystals, purified a.i.) with a melting point of 93 °C. The substance decomposes before boiling at 200 °C. It is only slightly volatile, with a vapour pressure of $2 \cdot 10^{-4}$ Pa (at 20 °C, by extrapolation) and Henry's law constant of $6.6 \cdot 10^{-2}$ Pa•m^3/mol. Tolylfluanid does not absorb visible or ultraviolet light above 290 nm. The water solubility is slight (1.04 mg/l at 20 °C and pH 4), and is independent of the pH. The value of pK could not be determined. The log K_{ow} is 3.9 at 20 °C. The solubility of tolylfluanid in acetone, acetonitrile, dichloromethane, dimethylsulfoxide, and ethylacetate exceeds 250 g/l, and the substance is readily or highly soluble other solvents tested; 1-octanol (16 g/l), 2-propanol (22 g/l), n-heptane (54 g/l), polyethylene glycol (56 g/l), xylene (190 g/l). The tests on flammability, explosive or oxidising properties gave negative results. No self ignition at temperatures up to melting point (93 °C)

Particle size distribution was characterized by two methods: In laser diffractometric analysis of technical substance the proportion of particles under 50 µm was in the range of 2% - 8%. In a continuous drop method, the mass-% under the cut-off diameter of 4µm ("alveolar") was 0.008%, under 10 µm ("thoracic") 0.032%. The third fraction ("inhalable"), which is the sum of the two fractions and of the fraction on the 3rd filter, was 0.63 mass-% (rel.std dev. 22 %), for which the upper limit or particle size characteristics were not determined. The study did not characterise the proportion under the particle size diameter of 50 µm.

2.1.3. Methods of Analysis

The methods of analysis of active substance as manufactured and for determination of impurities which are present at quantities > 0.1 g/kg in the active substance as manufactured

have been validated and shown to be sufficiently specific, linear, accurate and precise. The methods for residue analysis in different matrices (soil, surface water, potable water and air), as appropriate for the assessed uses, have been validated and shown to be sufficiently sensitive with respect to the levels of concern. However, a validated analytical method for sediment is not available

2.1.4. Intended Uses and Efficacy

Tolylfluanid has been evaluated for its proposed use as a wood preservative (PT8) for Hazard Class (HC) 2 and 3 (HC2: wood above ground, occasional wetting, protected from the weather, HC3: wood which is not covered and not in contact with ground, but exposed to weather). Tolylfluanid is applied in solvent based product formulations either in primers or incorporated in low binder containing paints (e.g. stains, /"lazur"/glazes). The applicant has informed later (5th December, 2007) that tolylfluanid needs a subsequent treatment with a coating if it is applied in a primer.

The intended uses of tolylfluanid containing solvent based products are for industrial/professional wood preservation (dipping) and wood preservation by brushing outdoors by professionals and amateurs.

Formulated wood preservatives contain between 0.3 and 0.8% tolylfluanid (technical). A 0.8% concentration can be regarded as a maximum concentration, which may be put into the market. For the Guide Recipe a concentration of 0.7% active substance was chosen as a realistic concentration which reflects the upper end of existing products in the EU market. Low concentrations such as 0.3% are only used in products containing also other active substances.

The effectiveness of tolylfluanid against wood-staining/blue stain fungi (e.g. *Aureobasidium pullulans* and *Sclerophoma pityophila*) has been proved sufficiently. The wood preservative product has been shown to be adequately effective against blue stain fungi with a tolylfuanid retention of 0.6 -1.4 g/m^2 in wood for Hazard Class 2 and 3. It should be noticed that this effectiveness against blue staining fungi has been generated and shown in brushing treatment study, although tolylfluanid containing products are also intended for dipping. However, it is concluded, that the efficacy data submitted is adequate to show effectiveness of tolylfluanid containing products in superficial treatment of wood, in general.

According to the applicant tolylfluanid has also effects against wood-rotting fungi at much higher concentrations and when combining tolylfluanid with other active substances such as tebuconazole and propiconazole. However, the effectiveness of the Guide Recipe against wood rotting fungi and moulds has not been proved in the tolylfluanid wood preservative risk assessment.

The intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.5. Resistance

According to the applicant due to the unspecific mode of action a development of resistance is neither to be expected nor has been ever observed. A literature search on resistance to

tolylfluanid and wood preservation was negative. The Fungicide Resistance Action Committee (FRAC) has listed (2003-06-02) tolylfluanid in group M5 (= multi site contact activity / sulphamides) together with the comment: "generally considered a low risk group with no signs of resistance developing to the majority of fungicides / No cross resistance between the group members".

2.1.6. Classification and Labelling

The former classification/labelling of the active substance tolylfluanid according to Annex I of Council Directive 67/548/EEC (28th ATP) is shown in Table 1.

Table 1. Former classification of tolylfluanid (28th ATP, Dir. 2001759/EC)

Classification	as in Directive 67/548/EEC
Class of danger	T: Toxic N: Dangerous for the environment
R-phrases	R 23: Toxic by inhalation R 36/37/38: Irritating to eyes, respiratory system and skin R 43: May cause sensitisation by skin contact; R 48/20:Harmful: danger of serious damage to health by prolonged exposure through inhalation. R 50/53:Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S-phrases	S 1/2:Keep locked up and out of the reach of children; S 24:Avoid contact with skin; S 26:Avoid contact with eyes; rinse immediately with plenty of water and seek medical advice; S 37: Wear suitable gloves; S 38:In case of insufficient ventilation, wear suitable respiratory equipment S 45: In case of an accident or if you feel unwell, seek medical advice immediately (show label where possible) S 60: This material and its container must be

	disposed of as hazardous waste; S 61: Avoid release to the environment. Refer to special instructions/Safety data sheets

As agreed in the Commission's Technical Committee on Classification and Labelling of Dangerous Substances in March 2005 and included in the 31st ATP, the current classification/labelling is given in Table 2 and 3. If tolylfluanid is not respirable to a toxicologically significant amount (containing < 0.1% (w/w) of particles with an aerodynamic diameter of below 50 μm, Index No.613-116-01-4), the classification shall be the following (see Table 2):

Table 2. Current classification of tolylfluanid (31st ATP, Dir. 2009/2/EC)

Classification	as in Directive 67/548/EEC
Class of danger	Xi: Irritant; N: Dangerous for the environment
R-phrases	R 36/37/38: Irritating to eyes, respiratory system and skin R 43: May cause sensitisation by skin contact; R 50: Very toxic to aquatic organisms Specific concentration limits (for environmental classification): C ≥ 20 %: Xi, N; R36/37/38-43-50 2,5 % ≤ C < 20 %: Xi, N; R43-50 1 % ≤ C < 2,5 %: Xi; R43
S-phrases	(S 2): Keep out of the reach of children; S 25: Avoid contact with eyes; S 36/37: Wear suitable protective clothing and gloves; S 46: If swallowed, seek medical advice immediately and show this container or label S 61: Avoid release to the environment. Refer to special instructions/Safety data sheets

If the substance is respirable to a toxicologically relevant amount (containing ≥ 0.1% (w/w) of particles with an aerodynamic diameter of below 50 µm, Index No. 613-116-00-7), the classification shall be the following (see Table 3):

Table 3. Current classification of tolylfluanid (31st ATP, Dir. 2009/2/EC)

Classification	as in Directive 67/548/EEC
Class of danger	T+: Very toxic N: Dangerous for the environment
R-phrases	R 26: Very toxic by inhalation; R 48/23: Toxic: danger of serious damage to health by prolonged exposure through inhalation; R 36/37/38: Irritating to eyes, respiratory system and skin; R 43: May cause sensitisation by skin contact; R 50: Very toxic to aquatic organisms Specific concentration limits (for environmental classification): C ≥ 20 %: T+, N; R26-36/37/38-43-48/23-50 10 % ≤ C < 20 %: T+, N; R26-43-48/23-50 7 % ≤ C < 10 %: T+, N; R26-43-48/20-50 2,5 % ≤ C < 7 %: T, N; R23-43-48/20-50 1 % ≤ C < 2,5 %: T; R23-43-48/20 0,1 % ≤ C < 1 %: Xn; R20
S-phrases	(S 1/2): Keep locked up and out of the reach of children; S 28: After contact with skin, wash immediately with plenty of (to be specified by the manufacturer); S 36/37/39: Wear suitable protective clothing, gloves and eye/face protection; S 45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible);

	S 61:Avoid release to the environment. Refer to special instructions/Safety data sheets; S 63: In case of accident by inhalation: remove casualty to fresh air and keep at rest Alternatively: S(1/2)-28-36/37/39-45-63-61

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification

Critical endpoints:

The critical effects of tolylfluanid in a 2-year rat oral study included histopathological changes in bone and teeth caused by fluoride. A chronic NOAEL of 18 mg/kg bw/day was deduced. At higher dose levels also increased liver and kidney weights, slightly increased thyroid follicular cell hyperplasia and adenomas were observed. Criteria for classification were not met.
In a rabbit teratogenicity study increased postimplantation loss, increased incidence of malformations and placental alterations, and maternal toxicity (slight impairment of body weight development) were observed. From the study a short-term NOAEL of 25 mg/kg bw/day was derived. However, the developmental effects and maternal toxicity were marginal, and criteria for classification were not met.

Other human health hazards:

Tolylfluanid by the oral route is extensively and rapidly absorbed. Oral and dermal toxicity is low. Toxicity during inhalation exposure was low to high which was related to the particle size leading to a differentiated proposal for classification i.e. tolylfluanid containing ≥ 0.1% particles < 50µm is classified as very toxic. Inhalation toxicity of liquid aerosol is low.

Tolylfluanid has irritating properties in both eyes and skin, and has sensitizing properties. Main effects during short term oral exposure were functional disturbance of the thyroid, increased liver weights and decreased liver enzyme levels in the rat and dog and slight histopathological changes in the kidney in the dog at high dose levels.

During inhalation exposure severe respiratory tract irritation including deaths was observed. Depending on the particle size, tolylfluanid containing ≥ 0.1% particles < 50µm is classified as toxic.
Tolylfluanid is neither genotoxic nor carcinogenic. There were no classification-relevant effects on reproductive or developmental toxicity. No evidence of neurotoxicity was observed.

Tolylfluanid is a source of fluoride. In addition to changes in bones and teeth on rats and mice, several other effects on test animals may have been caused by fluoride. In general in humans,

chronic exposure to high levels of fluoride may cause adverse effects in bones and teeth. Exposure to fluoride derived from tolylfluanid can be estimated from chronic exposure scenarios.

For a detailed summary of health hazards of tolylfluanid, see Document IIA, Chapter 3.11.

Toxicological reference doses and safety factors

For setting of acceptable levels of exposure, two reference doses for the systemic toxicity of tolylfluanid were defined, with relevance to the assessment of risks associated with exposure to a wood preservative. The reference values are applicable both to primary exposure in professional and non-professional use, and to secondary exposure with intentional or unintentional exposure to the treated products. The reference values are based on systemic NOAELs from oral dosage studies in experimental animals. No correction were used in calculations of systemic body doses. The safety factor of 100 was used in deriving the reference doses from values of NOAEL. The reference doses and the relevant NOAEL-values are summarised in Table 4.

Table 4: Toxicological reference doses

Study	**NOAEL** **mg/kg bw/day**	**Reference dose** **mg/kg bw/day**	**Exposure**	**Relevance for risk assessment**
2-year oral study, rat (Leser *et al*., 1996)	18	0.18 (chronic AOEL) 0.18	primary exposure: industrial/professional workers secondary chronic exposure	long-term exposure (most days per year, or repeated exposure)
teratogenicity study, rabbit (Holzum *et al*., 1991b)	25	0.25 (short term AOEL) 0.25	primary exposure: non-professional painters secondary acute exposure	acute exposure (a single dose or a few days of exposure)

Health Hazards of the Product

Health hazards of the representative product, the Guide Recipe JJT 3580, containing 0.7 % w/w of the active ingredient, were extrapolated from the toxicological properties of tolylfluanid and of the solvent, a substance of concern. A concentrated product containing 10 % w/w

tolylfluanid, for industrial/professional use only and diluted to the concentration of the ready-to-use dipping formulation before application, was also considered.

Tolylfluanid was a sensitising substance in animal studies, and labelling of the Guide Recipe JJT 3580 with **"Contains tolylfluanid: may cause an allergic reaction"** is proposed. Irritation reactions of skin, eyes and the respiratory system could arise from handling of product concentrates (containing up to 10 % w/w of tolylfluanid) for professional operators. However, for this subpopulation the use of protective equipment can be assumed.

Due to the defattening properties of the solvent, White Spirit, the following classification is proposed for the Guide Recipe JJT 3580: **R 66; Repeated exposure may cause skin dryness or cracking**. White Spirit is also a potential cause of neurological effects and long-term neurological deficits in humans, if repeatedly inhaled. However, the criteria for R67 were not met.

2.2.1.2. Exposure assessment and risk characterisation

Manufacturing of the active substance and formulation of the products were not covered in the evaluation by the RMS. However, a qualitative assessment of the worker exposures via inhalation and dermal routes has been carried out by the producer. As a result clothing requirements and other safety measures have been set.

Both primary and secondary exposure to tolylfluanid in humans were estimated. A concentration of 0.8 % w/w of tolylfluanid in the ready-to-use product was used in the calculations. Calculations were performed according to the recommendations of the TNsG – Human Exposure to Biocidal Product (2002) and the User Guidance (2002). The models are based to a great extent on data from UK HSE surveys. The detailed calculations are presented in document IIB. For the risk characterisation, the 75%-ile values were used. Basic parameters and assumptions in exposure assessment are given in Appendix I, Listing of the endpoints.

Dermal route is the main route of exposure. Exposure by inhalation route and by oral route are also considered in some scenarios. The bodyweight values are 60 kg for an adult to include also females, 15 kg for a child, and 10 kg for an infant.

In the primary exposure scenarios, the dermal absorption rate (71.19 %) used has been determined *in vitro* for tolylfluanid in the representative product Guide Recipe JJT 3580, and in secondary exposure scenarios the dermal absorption value of 10 % was used. The former value (71.19 %) is considered a very conservative value, and the latter is (10 %) is possibly a moderately conservative one.

Primary exposure

<u>Industrial/Professional exposure</u>

Primary exposure scenarios for professionals included operators in industrial/professional applications (dipping) and other professionals (painting by brushing). Scenarios of mixing and loading (prior to dipping, both by pouring and by pumping), cleaning of dipping tank, and handling of wet treated wood were later included.
There is no unacceptable risk for operators involved in wood treatment by dipping if PPE (suitable protective clothing, including gloves and footwear, and goggles) is used. Only dermal and inhalation routes of exposure were considered relevant. The margin of exposure, MOE, was 161 for dipping (with mixing and loading included in the model).

For the professional painting, gloves and skin protection (coverall) were assumed. Dermal and inhalational routes of exposure were considered relevant. With use of PPE, no unacceptable risk was indicated, and the MOE was 545.

In other primary professional scenarios the MOE was 234 or higher.

Non-professional exposure

Painting by brushing is the only application envisaged for non-professional users. Only dermal and inhalational routes of exposure were considered relevant. Assuming a clothing penetration value of 50 %, no risk was indicated with the MOE of 227 with gloves and the MOE of 114 without gloves. The use of gloves as the only form of protective garment reduces exposure to tolylfluanid. It can be assumed that amateurs not wearing PPE are at higher risk of becoming sensitised to tolylfluanid.

Conclusion – primary exposure: Tolylfluanid in wood preservation can be considered safe for professional users using PPE, and for non-professional users with or without PPE (gloves). Use of gloves is recommended for non-professional users.

Secondary exposure

Secondary exposure in a residential environment may result from professional and non-professional applications. Relevant scenarios involve skin contact and possible exposure by inhalation or by ingestion.

An acute secondary exposure to tolylfluanid can be anticipated for adults who work with treated wood (sanding treated wood posts, the MOE = 32 500) or for infants who may have oral contact with treated wood (chewing wood off-cut, the MOE = 301). Children are not considered to be at a risk.
Chronic secondary exposure scenarios include adults who cut or sand treated wood (the MOE = 12 000) or who clean work ware at home (the MOE = 2 300). Children may have repeated dermal contact to treated structures (the MOE = 8 600), whereas infants can be expected to have additional oral absorption after hand-to-mouth contact (the MOE = 780).

It can be concluded that the use of tolylfluanid-treated material does not pose a health risk for humans as a result of secondary exposure.

Combined exposure

For primary exposure, systemic doses from the dipping scenarios and cleaning of dipping tank can be summed up to yield 0.133 mg/kg bw/day resulting in the MOE of 135. It is not known if such combination of tasks is usual. No other combination of tasks can be calculated to result in unacceptable risk, either.

Adults are the only subpopulation who may reasonably experience both primary and secondary exposure to tolylfluanid. The secondary exposure adds negligible or small doses to the primary exposure. The systemic dose from the secondary exposure scenario "Adult cleaning work ware at home" brings the MOE to 150 only when added to that from the dipping scenario. Also, cleaning work ware at home by dipping operators is not expected to be normally done during the working day, and therefore summing of the these systemic doses does not seem appropriate. Hence no additional concern arises from the combination of exposures.

Other effects:

White Spirit (a substance of concern), the solvent in the representative product may lead to skin dryness or cracking due to the defattening properties, and it is also a potential cause of neurological effects and long-term neurological deficits in humans, if repeatedly inhaled. Therefore the dermal and inhalation exposure to the solvent should be minimised.

Fluoride: Maximum amounts of fluoride derived from tolylfluanid were estimated from two chronic exposure scenarios. In a primary exposure scenario for professional dipping, the calculated total amount of fluoride was 0.52mg (based on the 95 %-ile value), which is comparable to an estimated daily intake of fluoride (0.5 mg) in food and in drinking water. This amount is less than the daily recommended (by the UK Medical Research Council 2002) maximum addition of fluoride (1.5 mg) in the form of fluoride tablets for prevention of caries in children in areas of low levels of fluoride in drinking water. Adverse effects of fluoride in humans have been reported (IPCS Environmental Health Criteria No 227, 2002) at levels exceeding 6 mg. Hence no risk is indicated. However, in regions of high fluoride, chronic exposure to tolylfluanid of industrial/professional operators could be taken into consideration as a factor in increasing the body burden of fluoride.

In the chronic secondary exposure scenario of "infant playing on weathered (playground) structure and mouthing" the amount of fluoride was (0.013 mg, from 0.0013 mg/kg bw/day), which can be considered as negligible.

Especially for the primary exposure (dipping), the calculated amounts of fluoride (maximally circa 0.5 mg/day) derived from tolylfluanid, as well as the systemic doses of tolylfluanid, should be regarded as over-estimates, because the value of dermal absorption used for tolylfluanid is a highly conservative one.

In conclusion, fluoride from tolylfluanid used for wood preservation does not pose an unacceptable risk to humans.

2.2.1.3. Risk assessment of N,N-dimethylsulfamide (N,N-DMS)

Introduction: Tolylfluanid and its metabolite DMST were found, via a recently found degradation product, N,N-dimethylsulfamide, to yield N-nitrosodimethylamine (NDMA), in ozonation in treatment of water. The maximum maximum transformation efficiency of 32% (units of µg or µg/l) can be used in calculating of NDMA formation. NDMA is genotoxic, mutagenic and carcinogenic (Carc. Cat. 2). NDMA has been classified by IARC in Group 2A "probably carcinogenic to humans" (IARC, 1987). The risk assessment of N,N-dimethylsulfamide and of NDMA by the RMS has been included in a separate Risk Assessment report, as a supplementary part to tolylfluanid risk assessment. This document includes information from the applicant, and also information on NDMA which is based on information in WHO publications.

Physical and chemical properties of N,N-dimethylsulfamide and method of analysis: N,N-dimethylsulfamide is slightly to very slightly volatile (vapour pressure; 1.8×10^{-4} Pa and Henry's law constant: 1.6×10^{-7} Pa m^3/mol). The compound is moderately soluble in water (140 g/l). It has a negative octanol/water partition coefficient (- 0.8) and is, therefore, unlikely to bioaccumulate. Study on dissociation constant (10.6) was not conducted according to GLP. Method for the determination of N,N-dimethylsulfamide in surface water was acceptably validated. See also Listing of End Points, Section B.

Toxicological assessment of N,N-dimethylsulfamide: The acute toxicity of N,N-dimethylsulfamide was low in rat by the oral route (LD_{50} higher than 2000 mg/kg bw). In a 28-day study in rat, focal/multifocal cortical/medullary mineralization of kidney was increased in females at the highest dose level, 1000 mg/kg bw/day. Hence, it is not possible to determine a NOAEL or a LOAEL for the study with certainty. However, based on agreement of the TMI 08, a precautionary approach could be taken in interpreting the results of this study from which a NOAEL of 200 mg/kg/d could be derived. N,N-dimethylsulfamide was negative in *in vitro* gene mutation tests in bacterial and mammalian cells. N,N-dimethylsulfamide did not increase the micronucleus frequency in polychromatic erythrocytes in an *in vivo* micronucleus assay in mouse bone marrow. Very slight bone marrow toxicity was observed in this test, if any. Hence, it is obscure if the test substance has reached bone marrow. The opinion of the RMS was that result of the micronucleus test is equivocal and can not prove that N,N-dimethylsulfamide does not have any clastogenic or aneugenic properties. However, the TMI 08 concluded that the result of the test should be taken as negative. Conclusion: The information on properties of N,N-dimethylsulfamide does not suggest that the substance is hazardous to health. However, the hazard assessment is based on a limited set of studies. In the risk assessment the potential of the substance to transform into NDMA in ozonation is also taken into account.

Risk characterisation: The risk assessment of N,N-dimethylsulfamide is based on comparison of predicted concentrations of N,N-dimethylsulfamide with the drinking water standard and groundwater quality standard of 0.1 µg/l, as agreed in the TMI08. A) Surface water: N,N-

dimethylsulfamide can be found in surface water from the wood preservative use, especially from industrial use of wood preservatives. It can be estimated that the highest predicted concentration of N,N-dimethylsulfamide, 0.394 µg/l, in surface water does not pose an unacceptable risk to humans. If the water is directly intended for the abstraction of drinking water, which is, however, not very probable, the drinking water standard of 0.1 µg/l can be exceeded. Risk mitigation methods are needed and are available for this wood preservative use. B) Ground water: Predicted concentrations, with the highest value of ca 15 µg/l, of N,N-dimethylsulfamide in groundwater, from tolylfluanid in wood preservation (painting by brushing), exceed the limit value of 0.1 µg/l, and therefore contamination of groundwater can not be excluded when tolylfluanid is used in wood preservation. An unacceptable risk based on limited information on the health effects of N,N-dimethylsulfamide is not suggested. A toddler with a bodyweight of 10 kg and an estimated consumption of drinking water of 2 litre/day containing 15 µg/L of N,N-dimethylsulfamide would receive a dose of 3 µg/kg bw/day, which would be only ca 0.0015% of the proposed alternative NOAEL (200 mg/kg bw/day) from the 28 day oral study. Based on the limited information available, N,N-dimethylsulfamide as such in drinking water does not cause an unacceptable risk to human health, but emphasis should be put on the potential formation of a nitrosoamine, NDMA from N,N-dimethylsulfamide. The high mobility and persistency of N,N-dimethylsulfamide in water makes it a potential precursor of NDMA for a very long time. Hence contamination of groundwater and surface water can not be excluded.

Risk mitigation measures: There are some risk mitigation measures to reduce both leaching of the precursors of N,N-dimethylsulfamide from the treated wood (top-coating) or to reduce the amount of N,N-dimethylsulfamide in water (purification of water). However, top-coating of wood was calculated to be insuffient for the purpose. Purification of water has not been demonstrated to be sufficient or practical.

Conclusion on the risks of N,N-dimethylsulfamide: No practical risk mitigation methods exists that would bring the calculated level of N,N-dimethylsulfamide in groundwater or drinking water below 0.1 µg/l. Concentrations of N,N-dimethylsulfamide in surface water and especially in groundwater may exceed the drinking water standard and the groundwater quality standard of 0.1 µg/l. Hence, an unacceptable risk from the use of tolylfluanid as a wood preservative via drinking water can not be excluded. It was agreed in the TMI08 that drinking water limit value of 0.1 µg/l shall be used in the risk assessment.

2.2.1.4. Risk assessment of NDMA

Toxicological assessment of NDMA: The toxicological properties of NDMA are summarised in a separate risk assessment report (see also 2.2.1.3), based on information from WHO. Original studies were not evaluated by the RMS. NDMA is a genotoxic, mutagenic, and a carcinogenic substance. WHO has set a health based value (HBV) of 100 ng/l for NDMA in drinking water associated with an upper-bound excess lifetime cancer risk of 10^{-5}. NDMA has been classified by IARC in Group 2A “probably carcinogenic to humans” (IARC, 1987). Other sources of NDMA are also known to exist but these have not been taken into account in this assessment.

Exposure assessment: The assessment of NDMA is included in a separate risk assessment report (see also 2.2.1.3), together with the risk assessment of its precursor substance, N,N-dimethylsulfamide. Predicted concentrations of NDMA in water following ozonation, from wood preservative use of tolylfluanid, are compared with the drinking water standard and the groundwater quality standard of 0.1 µg/l.

Risk characterization: If groundwater containing N,N-dimethylsulfamide is ozonated, concentrations of NDMA can exceed (the calculated maximum value was 5.05 µg/l) also both the drinking water standard of 0.1 µg/l and the specific health based value (HBV) of 0.1 µg/l set for NDMA by the WHO. From only one focus scenario, where Time 2 was considered, concentration < 0.1 µg/l could be calculated. Hence, the possibility of formation of NDMA from N,N-dimethylsulfamide in ozonation during treatment of water leads to a significant concern. Although groundwater is seldom ozonated as such, ozone can be used for removing impurities from raw water, also in groundwater. In small municipalities, where surface water and groundwater are mixed, ozonation can take place after mixing.

Conclusion on the risks of NDMA: For the precursor, N,N-dimethylsulfamide, no practical risk mitigation methods exist that would bring the calculated level of N,N-dimethylsulfamide in groundwater or drinking water below 0.1 µg/l with certainty. Theoretical maximum concentrations of NDMA in drinking water may exceed the drinking water standard and the groundwater quality standard of 0.1 µg/l. Hence, an unacceptable risk from the use of tolylfluanid as a wood preservative via drinking water can not be excluded. It was agreed in the TMI08 that drinking water limit value of 0.1 µg/l shall be used in the risk assessment.

Ozonation of groundwater is not very common at present. However, in assessing of the risks it must be taken account that the precursor of NDMA, N,N-dimethylsulfamide, is a very persistent and mobile substance in water. The high toxicity (genotoxicity, mutagenicity and carcinogenity) of NDMA is well characterised in scientific literature.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Tolylfluanid and DMST are not ready biodegradable. Photodegradation of tolylfluanid and DMST in water is also very slow. Tolylfluanid hydrolyses rapidly in neutral and alkaline conditions (DT50 = 40 hours at pH 7 and 4.3 hours at pH 8 at 20 °C). DMST and N,N-dimethylsulfamide (N,N-DMS) are hydrolytically stable.

Based on the low vapour pressure tolylfluanid (2 x10^{-4} Pa, 20 °C), DMST (2.5 x 10^{-4} Pa, 20 °C) and N,N-DMS (1.8 x 10^{-6} h Pa at 20 °C) have a low tendency to volatilise. Tolylfluanid, however, could have a tendency to volatilise from water based on the Henry's law constant of 7.7 x 10^{-2} Pa x m^3 x mol^{-1}, but its hydrolysis is so rapid, that volatilisation is not of concern for the distribution of tolylfluanid in the environment. DMST and N,N-DMS have no tendency to volatilise from water based on their very low Henry´s law constants.

Due to the short chemical lifetime in air tolylfluanid and DMST are not expected to be carried in the gaseous phase over long distances or to accumulate in air.

Tolylfluanid is degraded very fast in the water/sediment studies. Tolylfluanid is metabolised by hydrolytic cleavage of the N-S bond to DMST, which in turn undergo oxidation to DMST-acid. Further quick cleavage of the benzoic acid moiety yields N,N-dimethylsulfamide (Figure 1). DT50 of tolylfluanid in water (dissipation) and total system (degradation) based on the water/sediment study carried out with **[N-methyl-^{14}C]-tolylfluanid** was 0.2-0.3 days. DT50 of DMST in water (dissipation), sediment (dissipation) and total system (degradation) was 15-23 days, 15-41 days and 18-48 days, respectively. The formation of N,N-dimethylsulfamide started very fast (during the first to 15 days) so that the maximum amount of N,N-dimethylsulfamide detected was **78%** (68.1% in water and 10.1% in sediment) at day 76 in Angel-Weiher and 61% (46.1% in water and 14.9% in sediment) at day 120 in Hoenniger-Weiher water/sediment system. N,N-dimethylsulfamide was found to be almost persistent in water/sediment system. The DT_{50} (dissipation) of N,N-DMS in water and in total system calculated based on the best fit kinetic were 967->1000 days and >1000 days, respectively.

DT50 (dissipation) of tolylfluanid in water, sediment and total system based on the water/sediment study carried out with **[phenyl-UL-^{14}C]-tolylfluanid** was 0.06-0.3 days, 0.1-0.2 days and 0.06-0.2 days, respectively. DT50 (dissipation) of DMST in water, sediment and total system was 42-76 days, 34-77 days and 44-81 days, respectively. N,N-dimethylsulfamide was not detected in the study carried out with [phenyl-UL-^{14}C]-tolylfluanid.

Degradation pathway of tolylfluanid in soil is similar to degradation pathway in aquatic systems (Figure 1). Tolylfluanid is rapidly degraded to DMST, which further is degraded to N,N-DMS mainly through DMST-benzoic acid. Based on the soil degradation study carried out with **[N-methyl-^{14}C]-tolylfluanid** geometric mean DT50 of tolylfluanid and DMST in soil is 0.59 days and 2.1 days, respectively. As in aquatic systems degradation of N,N-DMS in soil is very slow. Geometric mean DT50 of N,N-DMS is 153 days (at 20 °C, 55% MWHC). The maximum formation of N,N-DMS was up to 17.6- **23.1%** of the applied radioactivity. Although mineralization of tolylfluanid is rather high accounting for 33-44% during 120 days, the amount of bound residues is also high; 38-45% of the applied radioactivity.

DT50 of tolylfluanid in soil based on the soil degradation study carried out with **[phenyl-UL-^{14}C]-tolylfluanid** was 0.5-2.6 days. DT50 of DMST, only metabolite appearing >10%, was 1.3-6.7 days in soil. N,N-dimethylsulfamide was not detected in the study carried out with [phenyl-UL-^{14}C]-tolylfluanid.

K_{oc} of 2200 indicates a low mobility potential of tolylfluanid, whereas K_{oc} values of 56-118 for DMST indicates high mobility potential. N,N-DMS shows no adsorption to soil at all and therefore K_{oc} value was not possible to determine. N,N-DMS can be considered as a very mobile in soil. In the risk assessment K_{oc} of N,N-DMS was set to zero.

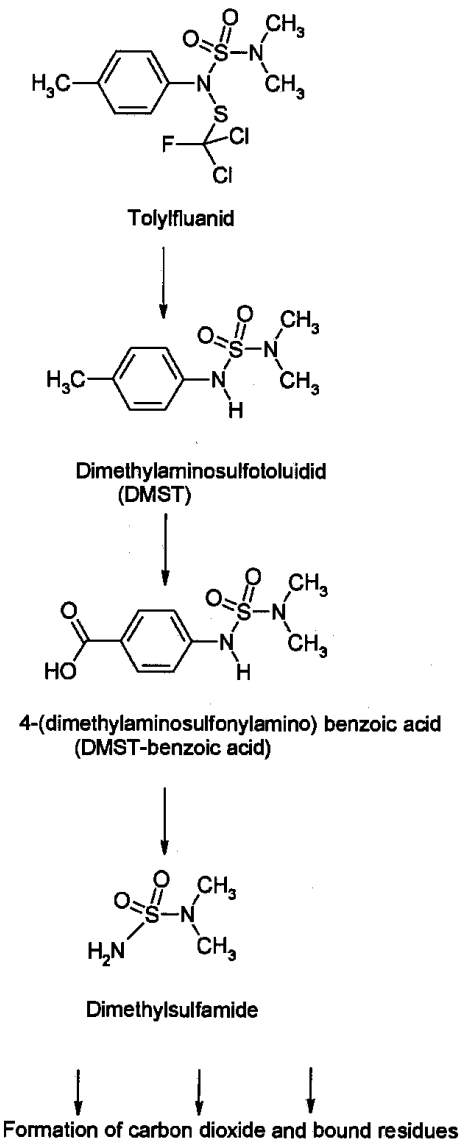


Figure 1. The main degradation pathway of tolylfluanid in soil and in water

Based on BCF value of 74 and log K_{ow} of 3.9 tolylfluanid show some potential for bioconcentration. DMST and N,N-DMS, however, are unlikely to bioaccumulate in organisms due to their hydrophilic properties (solubility of DMST and N,N-DMS in water is 677 mg/l and 140 g/l at pH 7 at 20 °C , respectively) and low K_{ow} values (for DMST:1.99 and for N,N-DMS: -0.8 at 20 °C).

The submitted literature search is considered sufficient and the findings of it support the conclusions made in Document IIA.

2.2.2.2. Effects assessment

Tolylfluanid and DMST are very toxic to aquatic organisms, whereas N,N-DMS is toxic. The following Predicted No-Effect Concentrations (PNEC) have been derived for tolylfluanid, DMST and N,N-DMS:

$PNEC_{water}$: 0.265 µg/l for tolylfluanid (derived from dichlofuanid by using read-across), 0.14 mg/l for DMST and 10 mg/l for N,N-DMS

$PNEC_{soil}$: 0.076 mg/kg ww for tolylfluanid, 0.196 mg/kg ww for DMST and 0.30 mg/kg ww for N,N-DMS.

The $PNEC_{STP:}$ 1 mg/l for tolylfluanid and 14.3 mg/l for DMST.

2.2.2.3. PBT assessment

Tolylfluanid, DMST and N,N-DMS do not fulfil the PBT criteria as given in the TGD, part II (2003). N,N-DMST fulfils VP (very persistent) criteria, because its DT50 (dissipation) in water is 967 ->1000 days.

2.2.2.4. Exposure assessment

The leaching values for treated wood used in the calculation of predicted environmental concentrations (PECs) are derived from a semi-field leaching study submitted on tolylfluanid. The ongoing study was started in October 2006. The study consists of 5 sampling periods where tolylfluanid and DMST were measured in leachate. Leaching of tolylfluanid was studied from primer product as well as from primer top coated with commercial top coat without tolylfluanid and top coat containing tolylfluanid. In the risk assessment when considering risk mitigation measures only top coat without tolylfluanid was considered.

The OECD Emission Scenario Document (ESD) used in the evaluation provides estimation of the local concentration based on the use of a wood preservative. Concerning PEC from production and formulation, and regional PECs the RMS makes the following conclusions. Only very local if any environmental exposure is expected from formulation processes of biocidal products containing tolylfluanid. Also otherwise contribution to the regional background concentrations of the active substance can be regarded as insignificant due to the anticipated very local emission patterns of the use of the biocidal product with soil as the main receiving compartment. Thus, all the regional PECs may be considered to be negligible and quantitative estimates of these are not relevant for the risk assessment. The following risk characterizations apply in local scale.

Based on the intended use of tolylfluanid in wood preservation the following OECD Emission Scenarios were used in the emission calculation of tolylfluanid and DMST:

1. Industrial application and storage containing dipping processes and storage place

2.Wood in-service treatment by amateurs and professional containing Fence, House, Noise barrier and Bridge over pond scenarios

3. *In situ* treatment by amateurs and professional containing Fence, House and Bridge over bond scenarios.

In calculation of PECs for N,N-DMS the main focus has been the human exposure via drinking water use, therefore only the following wood preservative scenarios, i.e. Industrial use (dipping and storage) as well as wood in-service; noise barrier scenario are used. PECs in groundwater were calculated according to the groundwater exposure assessment for wood preservatives guideline endorsed at the 24th Biocide CA-meeting by using FOCUS-PEARL 3.3.3 model.

2.2.2.5. Risk characterisation for the environment

Sewage treatment plant (STP)

Tolylfluanid and DMST do not pose unacceptable risk to STP.

Aquatic compartment

There is an unacceptable risk of tolylfluanid to the surface water from application plants via STP and emissions from the storage if tolylfluanid containing application solutions are not recycled.

Tolylfluanid causes unacceptable risk to aquatic organisms only in situ application of the bridge over pond scenario at day 1 (initial). Thereafter, there is no unacceptable risk to aquatic organisms. DMST does not cause unacceptable risk to aquatic compartment when tolylfluanid is used in wood preservation.

N,N-DMS does not cause unacceptable risk to aquatic organisms (calculated by using industrial use and wood in service noise barrier scenario).

Sediment risk assessment was not carried out for tolylfluanid and DMST as decided at the TMI07 (see justifications for that in DOC IIB Chapter 3.3.4).

Terrestrial compartment

Storage of treated wood poses no unacceptable risk of tolylfluanid, DMST or N,N-DMS to soil organisms. There is only unacceptable risk of tolylfluanid and DMST to soil organisms after in situ initial treatment at day 1. Thereafter, there is no risk to soil organisms.

N,N-DMS does not pose unacceptable risk to soil organisms when calculated by using house and fence in-service scenario as well as storage scenario.

There is no unacceptable risk of tolylfluanid to agricultural soil and grassland via application of STP sludge.

Groundwater used as drinking water

The groundwater concentrations of N,N-dimethylsulfamide calculated by the FOCUS-PEARL 3.3.3 model exceed the drinking water standard of 0.1 µg/l (Drinking water Directive 98/83/EC4) as well as the groundwater quality standard of 0.1 µg/l (Groundwater Directive 118/2006/EC5). The maximum concentration of N,N-dimethylsulfamide in the worst case scenario Jokioinen was 15 µg/l.

Atmosphere

Tolylfluanid, DMST and N,N-DMS are not expected to partition to the atmosphere to any significant extent due to their low vapour pressure and short chemical lifetime in air. Tolylfluanid is not expected to have a potential for long-range atmospheric transport or contribute to global warming, ozone depletion or acidification on the basis of its physical and chemical properties.

Risk for secondary poisoning

Tolylfluanid, DMST and N,N-DMS do not show a intrinsic potential for bioconcentration in organisms that could lead further to secondary poisoning. In addition, tolylfluanid is rapidly degraded in water indicating no need to assess this exposure route further.

Waste disposal stage

It is most unlikely that tolylfluanid containing biocidal product wastes will result in an unacceptable environmental risk during incineration under controlled conditions required in the waste legislation. It is also unlikely that tolylfluanid treated timber when disposed in a landfill site results in an environmental risk. Emissions of tolylfluanid from a landfill site can be assumed to be significantly less than that described for the house scenario for wood in service during period up to 15 years, which causes the highest emissions of tolylfluanid in soil.

Compliance with the environmental criteria for approval of active substance according to Annex VI of the Directive 98/8/EC

Tolylfluanid as such would fulfill the criteria for Annex I inclusion, but its degradation product N,N-DMS does not fulfill regarding the groundwater contamination. Drinking water standard of

4 Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption

5 Directive 2006/118/EC of the European Parliament and of the Council of 12 December 2006 on the protection of groundwater against pollution and deterioration

0.1 µg/l (Drinking water Directive 98/83/EC6) as well as the groundwater quality standard of 0.1 µg/l (Groundwater Directive 118/2006/EC7 are exceeded.

2.2.3. List of endpoints

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

3. PROPOSAL FOR DECISION

3.1. Background to the Decision

Tolylfluanid is requested for Annex I inclusion as a wood preservative to be used in use classes 2 and 3 by professional and non professional users. Based on the risk assessment tolylfluanid as such would fulfill the criteria for Annex I inclusion, but its degradation product N,N-dimethylsulfamide (N,N-DMS) and especially formation of NDMA during ozonation of drinking water raises a serious concern.

In wood preservative risk assessment of tolylfluanid the main focus has been the degradation product N,N-DMS (Risk assessment of N,N-DMS), found only a couple of years ago after extensive investigation of the increased nitrosoamine (NDMA) concentrations in ozonated Rhine water and after that in groundwater in agricultural areas in Germany. N,N-dimethylsulfamide was verified later to be the precursor of NDMA during ozonation.

NDMA is a genotoxic, mutagenic, and a carcinogenic substance. WHO has set a health based value (HBV) of 100 ng/l for NDMA in drinking water associated with an upper-bound excess lifetime cancer risk of 10^{-5}. Furthermore, the following intervention limits have been established: 10 ng/l (California), 9 ng/l (Ontario), 10 ng/l (Germany, UBA). Waters with concentrations higher that 200 ng/l are forbidden to be used as drinking water in California.

Because N,N-dimethylsulfamide does not cause unacceptable risk to aquatic or terrestrial organisms due to the wood preservative use, the risk assessment of N,N-DMS has been focused on human exposure of N,N-DMS and later NDMA through drinking water use. Relevant wood

6 Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption

7 Directive 2006/118/EC of the European Parliament and of the Council of 12 December 2006 on the protection of groundwater against pollution and deterioration

preservative scenarios have been used in calculations of PECs in the surface water and in groundwater.

Concentrations of N,N-dimethylsulfamide in surface water and especially in groundwater may exceed the drinking water standard and groundwater quality standard of 0.1 µg/l. Hence, an unacceptable risk from the use of tolylfluanid as a wood preservative via drinking water can not be excluded. It was agreed in the TMI08 that drinking water limit value of 0.1 µg/l shall be used in the risk assessment as reference value.

Although N,N-dimethylsulfamide based on limited information on its health effects does not seem to be hazardous to humans, it should be remembered that the possibility of the formation of NDMA during ozonation raises serious concern. Because N,N-dimethylsulfamide is very mobile and persistent in water it can be dispersed widely and will remain in water bodies for a very long time. Hence, contamination of groundwater and surface water can not be excluded.

If groundwater containing N,N-dimethylsulfamide is ozonated, concentrations of NDMA can exceed the drinking water standard of 0.1 µg/l and the specific health based value (HBV) of 0.1 µg/l set for NDMA by the WHO. Hence, the possibility of formation of NDMA from N,N-dimethylsulfamide in ozonation during treatment of water leads to a significant concern. Although groundwater is seldom ozonated as such, ozone can be used for removing impurities from raw water, also in groundwater. In small municipalities, where surface water and groundwater are mixed, ozonation can take place after mixing.

Following risk mitigation measures were considered to exclude the groundwater risk. However, after considering the practicability and feasibility of the possible measures, it was concluded that measures can not be considered sufficient enough.

1) Top coating

Although it was seen that top coating decreased the leaching of tolylfluanid from treated wood substantially (i.e. to 1.3- 6.5% of the retention), the PECs of N,N-dimethylsulfamide decreased much, but never under the drinking water limit value of 0.1 µg/l (agreed to be used for N,N-dimethylsulfamide in TMI08) in any of the FOCUS scenarios. Theoretical NDMA concentration was, however, below 0.1 µg/l in certain focus scenarios, e.g. in Sevilla.

Uncertainty to the use of top coating as one of the risk mitigation measures is related to the fact that a long-term effectiveness of top coating is not finally proved, although it has been seen that in the beginning, i.e. during the first two years leaching of tolylfluanid has decreased drastically compared to the primer leaching. The RMS is also of the opinion that the top coating requirement can be difficult to enforce. It could be possible to order mandatory top coating when wood is treated industrially, but for *in situ* brushing it can be difficult to control. According to the applicant and some Member Sates this would not be a problem, because the requirement for top coating can be given in the instructions for use and labels of the primer products, which has evidently been done for some primers already.

To summarise**,** top coating alone does not seem to reduce N,N-dimethylsulfamide and theoretical NDMA concentrations sufficiently in groundwater.

2) Water purification measures

According to the applicant (Klamroth *et al.* 2007) ozone is used for purification of water often in combination with other steps in water treatment. These steps, e.g. activated carbon filtering or sand filtering following ozonation, can lead into direct reduction of the level of NDMA in water in optimal conditions. In addition, reducing the level of N,N-dimethylsulfamide, the precursor of NDMA, in water by ion exchange resins or by other oxidation methods were reported to be possible ways to reduce the concentration of NDMA in water. According to the participant (Schmidt 2007) efficacy of several oxidation methods in removal of N,N-dimethylsulfamide from drinking water exceeded 85 %. However, the practicality and acceptability of these methods by waterworks remain uncertain. The high solubility in water of NDMA may hinder applicability of carbon filtering. The participant (Klamroth *et al* 2007) has referred to experiences where use of biologically active filters (sand filters or biologically active activated carbon filters) have been proposed to be effective in removing of NDMA from raw water in the Netherlands and in the UK, even though findings on considerable variability of effectiveness of NDMA removal by biodegradation was mentioned, too. The participant's report on the monitoring in the UK does not contain information on the transformation efficiency by ozone or on efficacy of reduction of levels of N,N-dimethylsulfamide in water purification process. The RMS has not been able to receive information from other sources to confirm the effectiveness of biological degradation of NDMA in activated carbon. A reduction in levels of NDMA could be explained by biological activity in carbon filters. Other purification mechanisms with poorly characterised properties in multistep purification processes are regarded possible.

Replacement of ozonation with treatment with other oxidants or disinfectants, as well as moderation of the ozonation process has been proposed by the participant as additional controlling measures. However, the RMS is not convinced if such approaches are sufficient or are seen practical by water authorities. The stability and the high mobility of N,N-dimethylsulfamide make it a candidate for a long-lasting impurity in both surface water and groundwater.

Due to the stability of N,N-dimethylsulfamide in water it can accumulate in sources of drinking water, which makes it a substance that should be regarded with a concern. The further technical development of water purification technology will remain an open question. The extent of use of ozone in future is unknown.

It should be borne in mind that Biocidal Products Directive regulates only placing on the market of biocides. Risk mitigation should therefore consist of measures directly linked to use of biocidal products. Consequently, it is beyond the administrative branch and the competence of the BPD authorities to regulate practices or techniques in waterworks.

3) Prohibition for use of tolylfluanid treated wood in groundwater protection areas

Prohibition of use of tolylfluanid treated wood in groundwater protection areas has been considered as one possible risk mitigation method. However, regional or European wide prohibition does not seem feasible. The concept of groundwater protection area does not exist in all European countries or it is not similar in different MS. Users of biocidal products or treated timber do not necessarily know if the place is situated on such an area. Therefore, this

type of prohibition is impossible to enforce.

3.2. Decision regarding Inclusion in Annex I

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

Minimum purity of the active substance in the biocidal product as placed on the market is 960 g/kg. Member states shall ensure that authorisations are subject to the following conditions:

(1) In view of the assumptions made during the risk assessment, products authorised for industrial use must be used with appropriate personal protective equipment, unless it can be demonstrated in the application for product authorisation that risks to industrial users can be reduced to an acceptable level by other means.

(2) In view of the risks identified for the soil and aquatic compartments, appropriate risk mitigation measures must be taken to protect those compartments. In particular, labels and/or safety-data sheets of products authorised for industrial use shall indicate that freshly treated timber must be stored after treatment under shelter or on impermeable hard standing to prevent direct losses to soil or water and that any losses must be collected for reuse or disposal.

(3) Products shall not be authorised for the *in situ* treatment of wood outdoors or for wood that will be exposed to weathering.

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

- Member States can only authorize tolylfluanid containing wood preservative products for Hazard Class 2 (wood above ground, occasional wetting, protected from the weather), because no safe use of tolylfluanid as a wood preservative for Hazard Class 3 as required in Article 5(1)(b)(iv) of Directive 98/8/EC was possible to demonstrate based on the dossier submitted for review program.

- Products containing tolylfluanid may be used in the preventative treatment of wood by brushing and industrial dipping for wooden constructions.

- When industrial/professional operators use products they must wear the appropriate personal protective equipment: protective goggles, chemical resistant rubber gloves, protective clothing and shoes.

- For non-professionals, hand protection (gloves) during painting is recommended.
- Extension of the use pattern beyond Hazard Class 2 will require a re-evaluation of the acceptance of tolylfluanid in order to establish whether the proposed extensions of use can satisfy the requirements of Article 10(1) and 5(1) of Directive 98/8/EC.

- According to the EU waste legislation waste from wood preservative products and application solutions are considered hazardous waste. Therefore, application solutions must be collected and reused or disposed of as hazardous waste and they must not be released to soil, surface water or any kind of sewer[8].

- The efficacy of the individual products shall be demonstrated prior to product authorisation at the Member State level.

- Based on Ann. V of the directive 1999/45/EC, preparations not classified as sensitising but containing at least one sensitising substance in a concentration ≥0.1% must bear the inscription 'Contains (name of sensitising substance). May produce an allergic reaction.'

3.4. Requirement for further information

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

3.5. Updating this Assessment Report

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

8 These requirements may actually be determined in detail in the environmental permits of the application plants on the basis of the Council Directive 96/61/EC on Integrated Pollution Prevention and Control (IPPC) but should be listed in the instructions for use of a biocidal product.

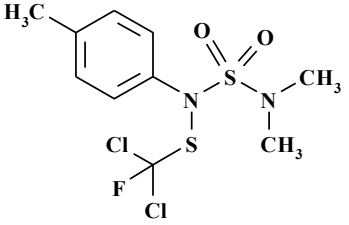
Appendix I: Listing of end points

SECTION A. Tolylfluanid and DMST

Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling of tolylfluanid including data from N,N-dimethyl-N'-p-tolylsulphamide (DMST)

Active substance (ISO Common Name)	Tolylfluanid
Function (*e.g.* fungicide)	Fungicide
Rapporteur Member State	Finland

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	N-(Dichlorofluoromethylthio)-N',N'-dimethyl-N-p-tolylsulfamide
Chemical name (CA)	Methanesulfenamide, 1,1-dichloro-N-[(dimethylamino)sulfonyl]-1-fluoro-N-(4-methylphenyl)-
CAS No	731-27-1
EC No	211-986-9
Other substance No.	CIPAC No. 275
Minimum purity of the active substance as manufactured (g/kg or g/l)	≥ 960 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	
Molecular formula	$C_{10}H_{13}Cl_2FN_2O_2S_2$
Molecular mass	347.3
Structural formula	

Physical and chemical properties (Annex IIA, point III., unless otherwise indicated)

Melting point (state purity)	93°C (purity:99.9%)
Boiling point (state purity)	Not measurable, substance decomposes at > 200°C (purity:99.9%)
Temperature of decomposition	DTA: Exothermic reaction above 200 °C. TGA-measurement: Weight loss observed above 150 °C under air and nitrogen. (purity:99.9%)
Appearance (state purity)	Physical state: solid Colour: colourless crystals (purified a.i.) colourless chrystalline powder with lumpy parts (techn.) (purities not specified) Odour: odourless (purified a.i.). Weak characteristic acidulous, musty smell (techn.) (purities not specified)
Relative density (state purity)	1.530 g/cm³ at 20°C (purity: 99.9%)
Surface tension	70 mN/m at 20°C (measurements in the range of concentrations of 0.64-0.96 mg/l); not surface active (99.0%)
Vapour pressure (in Pa, state temperature)	2 x 10^{-4} Pa at 20°C (extrapolated); 4 x 10^{-4} Pa at 25°C (extrapolated) (purity: 99.9%)
Henry's law constant (Pa m^3 mol^{-1})	6.6 × 10^{-2} Pa· m³· mol^{-1}
Solubility in water (g/l or mg/l, state temperature)	pH__5____: see below (pH 4) pH__9____: see below (pH 4) pH__4____: 0.65 mg/l at 10°C, 1.04 mg/l at 20°C, 1.52 mg/l at 30°C; (purity:99.9%) The solubility in water is independent from pH in the range of pH 4 to pH 9.
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	Results at 20ºC (purity 99.0%): 1-octanol 16 g/l 2-propanol 22 /l n-heptane 54 g/l polyethylene glycol 56 g/l xylene 190 g/l acetone > 250 g/l acetonitrile > 250 g/l dichloromethane > 250 g/l dimethylsulfoxide > 250 g/l ethylacetate > 250 g/l
Stability in organic solvents used in biocidal products including relevant breakdown products	Tolylfluanid was stable for 8 weeks at 40 °C in

(IIIA, point III.2)	a test for storage stability of a solvent-based wood preservative
Partition coefficient (log P_{OW}) (state temperature)	Log K_{ow} = 3.9 at 20 °C (99.9%) This value is considered as independent of pH, in the pH range of 4 -9
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	pH 9: DT_{50} (10°C) = 1.6 h DT_{50} (20°C) = 0.49 h DT_{50} (25°C) = 0.29 h
	pH 7: DT_{50} (10°C) = 161 h DT_{50} (20°C) = 40.0 h DT_{50} (25°C) = 20.5 h
	pH 4: DT_{50} (10°C) = 3980 h DT_{50} (20°C) = 961 h DT_{50} (25°C) = 490 h
	DMST, a metabolite of tolylfluanid, is hydrolytically stable.
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	Tolylfluanid shows in aqueous solvents neither acidic nor basic properties (in the range pH 4 to pH 9). pK value is not possible to specify. (99.9%)
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	UV/VS measured in methanol gave absorption maximum at 210 nm. No absorbance above 290 nm. (99.9%)
Photostability (DT_{50}) (aqueous, sunlight, state pH) (point VII.7.6.2.2)	As the UV absorption data showed that in aqueous solution tolylfluanid did not absorb any light at wavelengths above 290 nm, the molar extinction coefficient was calculated to be <10. Therefore, the determination of the quantum yield was not required. Even under assumption of a quantum yield of 1 the assessment of the environmental half-life by means of computer models would yield values of several years.
Quantum yield of direct phototransformation in water at Σ > 290 nm (point VII.7.6.2.2)	See above
Flammability	The test substance is not highly flammable. No self ignition at temperatures up to melting point (93 °C) (97.7%)

Explosive properties	Test substance is not explosive. (97.1%)
Oxidizing properties	Test substance is not oxidizing (97.1%)

Physical and chemical properties of the metabolite N,N-dimethyl-N'-p-tolylsulphamide (DMST)

Vapour pressure	2.5×10^{-4} Pa at 20 °C (94.9%) (extrapolated)
Henry´s Law Constant	7.7E-05 $Pa \cdot m^3 \cdot mol^{-1}$ at 20 °C
Solubility in water	677 mg/l at 20 °C (94.95%)
Partition coefficient n-octanol/water	log K_{ow} = 1.99 at 20 °C (99.8%)

Classification and proposed labelling (Annex IIA, point IX.)

with regard to physical/chemical data	No classification required
with regard to toxicological data	See document I, Chapter 2.5
with regard to fate and behaviour data	No classification required
with regard to ecotoxicological data	N, R50

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1) Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	Tolylfluanid and organic impurities quantified by reverse phase HPLC (Spherisorb ODS 2, 125 mm x 4.0 mm, 3 µm) with gradient elution and using external standardisation and DAD detector. Inorganic substances: titration of sample solution with silver nitrate solution to ascertain the chloride content and the content of magnesium is determined from an external standard calibration curve by Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES).

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	Soil samples were cleaned up by GPC and purified (not for DMST) using silica gel columns. The concentrated extracts were analysed using capillary gas chromatography (DB-5 MS) with mass selective

	detection (MSD). The MS ion m/z 238, 137 and 181 is used for quantification. For DMST MS ion m/z 214 and 106 is used for quantification. LC-MS/MS was additionally used for DMST for confirmation with m/z 106. LOQ for tolylfluanid and DMST in soil is 0.01 mg/kg.
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Air is passed through Tenax- or XAD-2 adsorption tubes with a rate of 2 l/min for 6 hours. The adsorbed active substance is extracted with n-butylacetate and determined by gas chromatography using a capillary column and a N/P-specific detector. Confirmatory method for quantitation of tolylfluanid residues in air is based on gas chromatography using a capillary column and a mass selective detector (MSD). In the selected ion monitoring mode, two individual ions at m/z = 137 and 238 are used for detection. Lower limit of quantification: 0.01 mg a.i. /m^3 air.
Water (principle of method and LOQ) (Annex IIA, point 4.2)	Prior to analysis formic acid is added to the drinking and surface water samples to a final concentration of 1 ml/l. Acidified samples are directly injected into the HPLC-MS/MS. Residues of tolylfluanid and DMST were determined by HPLC (Phenomenex Aqua®, 150 mm x 2 mm, 5 µm column; gradient eluation) using turbo-ionspray interface and mass selective detector (MS/MS). The method was validated for two mass transitions of tolylfluanid (m/z 346.9 → 237.8 and m/z 346.9 → 137.0) as well as DMST (m/z 214.9 → 106.0 and m/z 214.9 → 79.0). LOQ for tolylfluanid and DMST in surface and drinking water is 0.05 µg/l.
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	n.a.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	n.a.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	n.a.
Sediment	Analytical methods developed and validated for soil(s) can be used for sediments without or with only marginal modifications which may also be necessary for individual soils. It is a matter of pre-validation of a method prior using it for sample analysis to figure out its suitability and to determine adjustments which are necessary to fulfill the acceptance criteria for validation.

Chapter 3: Impact on Human Health - Tolylfluanid

Absorption, distribution, metabolism and excretion in mammals (Annex IIA, point 6.2)

Rate and extent of oral absorption:	Rat: ^{14}C ring labelled tolylfluanid: 95%; t_{max} in plasma < 3 hours
	Rat: ^{14}C labelled fluorodichloromethyl sulphenyl group: 70–80%; t_{max} in plasma < 3 hours
Rate and extent of dermal absorption:	Final agreement on tolylfuanid as a plant protection product states that the dermal absorption is 5 % for the concentrate and 7 % for the 1:100 dilution (see DocIIA). Based on this, **10 % can be used** for dermal absorption in calculations of dermal absorption in the absence of solvent, e.g. in secondary exposure, as a moderately conservative value**.** In vitro dermal absorption study in human epidermis using **a mineral-oil based formulation** of tolylfluanid (0.7% by weight) was applied for 6 h. The absorbed dose after 24 h was **71.19%.**
Distribution:	Highest concentrations in the excretory and metabolically active tissues (liver and kidney). A high relative concentration was also found in thyroid of male rats.
Potential for accumulation:	No. Tolylfluanid was not found to accumulate in the carcass or carcass minus gastrointestinal tract.
Rate and extent of excretion:	Renal excretion (48 h): 50-60% ([dichloro-fluoromethyl-^{14}C]) and roughly 60-90% ([phenyl-UL-^{14}C]) of the administered radioactivity. Biliary excretion (48 h): 22-30% ([dichloro-fluoromethyl-^{14}C]) and 12-36% ([phenyl-UL-^{14}C]) of the administered radioactivity.
Toxicologically significant metabolite	Dimethylaminosulfotoluidide (DMST, N,N-dimethyl-N'-(4-methylphenyl)-sulfamide)

Acute toxicity (Annex IIA, point 6.1)

Rat LD_{50} oral	> 5000 mg/kg bw (males + females)
Rat LD_{50} dermal	> 5000 mg/kg bw (males + females)

Rat LC_{50} inhalation	Micronized dust, MMAD 2.1-2.5 µm: 200/160 mg/m^3/4 h (m/f) Technical dust**,** MMAD: 16.8-19.8 µm: > 1038 mg/m^3/4 h (m+f) Liquid aerosol, MMAD: 3.39 ± 1.96 µm: > 770 mg/m^3 air a.i./4h (m+f)
Skin irritation	Irritating to skin
Eye irritation	Irritating to eyes
Skin sensitization (test method used and result)	Sensitising (Magnusson-Kligman test)

Repeated dose toxicity (Annex IIA, point 6.3)

Species/ target / critical effect	Dog – liver (weight increase, histopathological alterations), kidney (nephropathy and disturbance of kidney function), thyroid (increased weight)
Lowest relevant oral NOAEL (short term)	33 mg/kg bw/day (subchronic dog)
Lowest relevant oral NOAEL (long term)	18 mg/kg bw/day (two-year rat)
Lowest relevant dermal NOAEL	No systemic effects were reported at 300 mg/kg bw/day (the highest dose tested). The NOAEL for topical effects: < 1 mg/kg bw/day (subacute rabbit)
Lowest relevant inhalation NOAEL	1 mg/m³ (4 weeks, rat)

Genotoxicity (Annex IIA, point 6.6)	Tolylfluanid is not proposed to be classified as mutagenic, based on the overall *in vivo* data pointing towards negative results, although some clear or equivocal genotoxicity test results were encountered in the sole acceptable *in vitro* chromosome aberration tests and in some of the tests for gene mutations in mammalian cells.

Carcinogenicity (Annex IIA, point 6.4)

Species/type of tumour	Rat / thyroidal follicular cell adenoma (not relevant for humans, rat-specific aetiology)

lowest dose with tumours	504–584 mg/kg bw/day

Reproductive toxicity (Annex IIA, point 6.8)

Species/ Reproduction target / critical effect	Rat, two-generation. Pups, reduced body weight and spleen weight
Lowest relevant reproductive NOAEL	14 - 31.5 mg/kg bw/day
Species/Developmental target / critical effect	Rabbit / Embryo (teratogenicity): increased resorptions; foetuses: increased number of malformations; does: hepatotoxicity
Lowest relevant developmental NOAEL	25 mg/kg bw/day
Species/Developmental target / critical effect	Rat (teratogenicity, 2nd spec): developmental effects
Lowest relevant developmental NOAEL	≥ 1000 mg/kg bw/day

Neurotoxicity / Delayed neurotoxicity (Annex IIIA, point VI.1)

Species/ target/critical effect	Tolylfluanid did not show any signs of delayed neurotoxicity in subchronic or chronic studies with repeated dosage.
Lowest relevant developmental NOAEL / LOAEL.	≥ 620 mg/kg bw/day (subchronic rat)

Other toxicological studies (Annex IIIA, VI/XI)

.....	No indications for special concern.

Medical data (Annex IIA, point 6.9)

.....	A few cases of allergic skin reactions are described among manufacturing plant personnel. As these occurred at plants where a structurally related substances are produced and formulated, the reactions can not be attributed only to tolylfluanid.

Summary (Annex IIA, point 6.10)

	Value	Study	Safety factor
ADI (if residues in food or feed)	Not relevant		
AOEL (Operator/Worker Exposure)	0.25 mg/kg bw/day	rabbit teratogenicity	100
	0.18 mg/kg	2-year rat oral	100

	bw/day		
Drinking water limit	Not relevant		
ARfD (acute reference dose)	Not relevant		

Acceptable exposure scenarios (including method of calculation)

Primary exposure	
Ind/prof. mixing and loading Mixing and loading, Model 7 Concentrate contains 10% of a.s to be diluted to 0.8% in use dipping fluid One event per day of 22 min duration by pouring, 32 min by pumping PPE: suitable coverall, protective gloves and footwear, eye/face protection (goggles)	Total systemic exposure: 0.027 mg/kg bw /day MOE : 667 (by pouring) Total systemic exposure: 0.077 mg/kg bw /day MOE : 234 (by pumping)
Application: **Industrial/professional dipping, with mixing + loading** Dipping, Model 1 One dipping event/day, 30 min /event PPE: suitable coverall, protective gloves and footwear, eye/face protection (goggles)	Total systemic exposure: 0.112 mg/kg bw /day MOE : 161
Industrial/professional cleaning of the dipping tank Handling Model 1 Infrequent cleaning, for up to 180 min during the task PPE: suitable coverall, chemically resistant gloves and footwear, eye/face protection (goggles)	Total systemic exposure: 0.0207 mg/kg bw /day MOE : 870
Handling of treated wet timber, Handling Model 1 Intermittent handling of wet treated wood for up to 180 min/day PPE: suitable coverall, protective gloves and footwear	Total systemic exposure: 0.021 mg/kg bw /day MOE : 857
Professional painting by brushing + cleaning of brush Consumer Product Painting Model 3	Total systemic exposure: 0.033 mg/kg bw /day MOE : 545

Product with 0.8 % a.s. One event of 155 min/day PPE: suitable protective gloves, footwear and a coverall	
Non-professional painting by brushing + cleaning of a brush Consumer Product Painting Model 3 Product with 0.8% a.s. One event of 155 min/day PPE: none	Total systemic exposure: 0.22 mg/kg bw /day MOE : 114
Non-professional painting by brushing + cleaning of a brush Consumer Product Painting Model 3 Product with 0.8% a.s. One event of 155 min/day PPE: gloves	Total systemic exposure: 0.11 mg/kg bw /day MOE : 227
Secondary exposure as a result of use	
Acute phase	MOE: Adult (sanding wood): 32 500 Child: not relevant Infant (chewing wood cut-off): 301
Chronic phase	MOE: Adult (professional sanding): 12 000 Adult (cleaning work ware): 2 300 Child (playing on playground structure): 8 600 Infant (playing on weathered playground structure and mouthing, modified): 780

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	Tolylfluanid: pH 9: DT_{50} (10°C) = 1.6 h DT_{50} (20°C) = 0.49 h DT_{50} (25°C) = 0.29 h
	Tolylfluanid: pH 7: DT_{50}(10°C)=161 h DT_{50}(20°C)=40.0 h

	DT_{50} (25°C) = 20.5 h
	Tolylfluanid: pH 4: DT_{50} (10°C) = 3980 h DT_{50} (20°C) = 961 h DT_{50} (25°C) = 490 h
	DMST is hydrolytically stable.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Tolylfluanid does not absorb any light at wavelengths above 290 nm. It is not degradable by direct photodegradation in water.
Readily biodegradable (yes/no)	No
Biodegradation in seawater	n.a.
Non-extractable residues	Water/sediment study carried out with [phenyl-UL-14C]-tolylfluanid: 34- 40.1% after 120 days
Distribution in water / sediment systems (active substance)	<u>Water/sediment study carried out with [N-Methyl-^{14}C]-tolylfluanid (at 20 °C):</u> Tolylfluanid DT50water (dissip.) 0.2-0.3 days Tolylfluanid DT50sediment(dis.) not evaluable Tolylfluanid DT50system (degr.) 0.2-0.3 days <u>Water/sediment study carried out with [phenyl-UL-14C]-tolylfluanid at 20 °C, dissipation values:</u> Tolylfluanid DT50water1.4-6 hours (0.06-0.3d) Tolylfluanid DT50sediment 2.6-4.8 hours (0.1-0.2 d) Tolylfluanid DT50total system 1.5-5 hours (0.06-0.2 d) ➔ DT50 of 6 hours is used in the risk assessment as a worst case value in calculation of tolylfluanid PEC in water. Converted to 12 °C **DT50 of 11.38 hours** was derived.
Distribution in water / sediment systems (metabolites)	<u>Water/sediment study carried out with [N-methyl-^{14}C]-tolylfluanid (20 °C):</u> DMST DT50 water (dissipation) 15-23 days DMST DT50 sediment (dissipation) 15-41 days DMST DT50 system (degradation) 18-48 days N,N-DMS DT50 water (dissip) 967->1000 days N,N-DMS DT50 sediment (dis.) not evaluable N,N-DMS DT50system(disp.)1000->1000 days <u>Water/sediment study carried out with [phenyl-UL-^{14}C]-tolylfluanid (20 °C) dissipation values:</u> DMST DT50 water 42.1-75.8 days

	DMST DT50 sediment 33.9-76.5 days DMST DT50 system 43.6-81.1 days ➔ DT50 of 75.8 days is used in the risk assessment as a worst case value in calculation of DMST PEC in water. Converted to 12 °C **DT50 of 143.75 days** was derived.

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

Mineralization (aerobic)	[N-methyl -^{14}C]-tolylfluanid soil degradation study 20°C, 120 days, 55% MWHC: 33-44.2% [phenyl-UL-^{14}C]-tolylfluanid soil degradation study 22°C, 40% WHC, 99 days: 25-40 %
Laboratory studies (range or median, with number of measurements, with regression coefficient)	<u>[N-methyl -^{14}C]-tolylfluanid soil degradation study:</u> Tolylfluanid DT_{50lab} (20°C, aerobic): **geometric mean= 0.59 days** (calculated from the DT50 values from 4 different soils 0.74, 0.73,0.29, 0.80 days) DMST DT_{50lab} (20°C, aerobic): **geometric mean=2.1 days** (calculated from the DT50 values from 4 different soils 2.5, 2,9, 2.2, 1.2 days) DMST-acid DT_{50lab} (20°C, aerobic): **geometric mean=1.4 days** (calculated from the DT50 values from 4 different soils 1.4, 2.2, 1.1, 1.3 days) N,N-DMS DT_{50lab} (20°C, aerobic): **geometric mean=153 days** (calculated from the DT50 values from 4 different soils 122, 136, 47, 699 days) ➔the geometric mean DT50 of 127 days (normalized to 100% field capacity) is used in the risk assessment in calculation of N,N-DMS PEC in groundwater. ➔the geometric mean DT50 of 153 days is used in the risk assessment in calculation of PEC soil of N,N-DMS <u>[phenyl-UL-^{14}C]-tolylfluanid soil degradation study:</u> Tolylfluanid DT50 (20 °C, aerobic): 0.5-2.6 days DMST DT50 (20 °C, aerobic): 1.3-6.7 days ➔For the calculation of PEC soil for tolylfluanid the longest DT50 of 2.2 days (22 °C) in soil was used in the risk assessment as a worst case value. Converted to 12°C **DT50 of 4.9 days** was derived. ➔For the calculation of PEC soil for DMST the longest DT50 of 5.7 days (22 °C) in soil was used in the risk assessment as a worst case value. Converted to 12°C **DT50 of 12.69 days** was derived.

	DT_{90lab} (20°C, aerobic):
	DT_{90lab} (20°C, aerobic):
	DT_{50lab} (10°C, aerobic):
	DT_{50lab} (10°C, aerobic):
	DT_{50lab} (20°C, anaerobic):
	degradation in the saturated zone:
Field studies (state location, range or median with number of measurements)	DT_{50f}:
	DT_{90f}:
Anaerobic degradation	n.a.
Soil photolysis	
Non-extractable residues	Bound residues: 38.1-45.1% in soil degradation study carried out with [N-methyl -^{14}C]-tolylfluanid Bound residues: 52-72% in soil degradation study carried out with [phenyl-UL-^{14}C]-tolylfluanid
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	
Soil accumulation and plateau concentration	-

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

Ka , Kd	Tolylfluanid: K_{oc} = 2220, log K_{oc} = 3.346
Ka_{oc} , Kd_{oc}	DMST: K_{oc}=56-118, arithmetic mean 76.4
pH dependence (yes / no) (if yes type of dependence)	➔Koc of 2200 for tolylfluanid and 76.4 for DMST are used in EUSES for calculation of PECs agricultural soil and grassland from the application of STP sludge.

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

Direct photolysis in air	n.a.
Quantum yield of direct photolysis	DT_{50}: The half-life of tolylfluanid in air was calculated to be 7.2 hours corresponding to a chemical lifetime in air of 10.4 hours.
Photo-oxidative degradation in air	Atkinson Model calculation (AOPWIN1.55a,1.87): DT50=7.2 hours, corresponding chemical lifetime of 10.4 hours in air (Tolylfluanid) DT50=2.4 hours, corresponding chemical lifetime of 3.3. hour in air (DMST)
Volatilization	2 x 10^{-4} Pa at 20°C (extrapolated) (Tolylfluanid)

6.6×10^{-2} Pa· m³· mol^{-1} (Tolyfluanid)
2.5×10^{-4} Pa at 20°C (extrapolated) (DMST)
7.7×10^{-5} Pa· m³· mol^{-1} (DMST)

Monitoring data, if available (Annex VI, para. 44)

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) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	Endpoint	Toxicity
Fish			
Rainbow trout (*Oncorhynchus mykiss*)	96 hours	Mortality, LC_{50}	0.016 mg/l (Tolylfluanid) 35 mg/l (DMST)
Fathead minnow (*Pimephales promelas*)	33 days	Reproduction, NOEC	0.004 mg/l (Dichlofluanid) >10 mg/l (DMST)
Invertebrates			
Daphnia magna	48 hours	Mortality, LC_{50}	0.19 mg/l (Tolylfluanid) 31 mg/l (DMST)
	21 days	Reproduction, NOEC	0.00265 mg/l (Dichlofluanid)
Algae			
Green alga (*Selenastrum capricornutum*)	72 hours	Growth inhibition, NOE_rC, E_rC_{50}	Tolylfluanid: NOErC=0.040 mg/l ErC_{50}=0.4 mg/l DMST: NOErC=10 mg/l ErC_{50}>71.2 mg/l
Microorganisms			

Activated sludge (mixed population)	3 hours	Oxygen consumption	Tolylfluanid: EC_{50}=230 mg/l, EC_{10}=21, Conclusion: NOEC>solubility of tolylfluanid, i.e.1.0 mg/l. DMST: EC_{10}= 143 mg/l

Effects on earthworms or other soil non-target organisms

Acute toxicity to …….. (Annex IIIA, point XIII.3.2)	Earthworm *(Eisenia fetida)*: LC_{50} (14 days) > 78.5 mg/kg ww (Tolylfluanid)
Reproductive toxicity to …… (Annex IIIA, point XIII.3.2)	Earthworm *(Eisenia fetida)*: NOEC (56 days) = 3.8 mg /kg ww (Tolylfluanid) NOEC (56 days)=9.8 mg/kg ww (DMST)

Effects on soil micro-organisms (Annex IIA, point 7.4)

Nitrogen mineralization	NOEC (28 days)=3.3 mg/kg ww (Tolylfluanid) NOEC (28 days)=14.1 mg/kg ww (DMST)
Carbon mineralization	NOEC (28 days)=3.3 mg/kg ww (Tolylfluanid)

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	n.a.
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	n.a.
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	n.a.
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	n.a.

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	n.a.

Acute contact toxicity	n.a.

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	n.a.
Acute contact toxicity	n.a.
Acute toxicity to ……..	n.a.

Bioconcentration (Annex IIA, point 7.5)

Bioconcentration factor (BCF)	Tolylfluanid: edible: 55, whole fish: 74
Depuration time(DT_{50}) (DT_{90})	Tolylfluanid: DT50 [days]: edible: 0.29, whole fish: 0.38
Level of metabolites (%) in organisms accounting for > 10 % of residues	

SECTION B. N,N-dimethylsulfamide

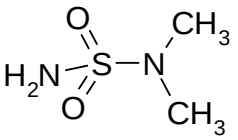
End Points of the metabolite N,N-dimethylsulfamide

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

Active substance (ISO Common Name)	N,N-dimethylsulfamide
Product-type	

Identity

Chemical name (IUPAC)	
Chemical name (CA)	Sulfamide, N,N-dimethyl-
CAS No	3984-14-3
EC No	
Other substance No.	

Minimum purity of the active substance as manufactured (g/kg or g/l)	
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	
Molecular formula	C2 H8 N2 O2 S
Molecular mass	124.16
Structural formula	

Physical and chemical properties

Vapour pressure (in Pa, state temperature)	1.8 x 10^{-4} Pa at 20°C 7.2 x 10^{-4} Pa at 25°C (98.1%)
Henry's law constant (Pa m^3 mol^{-1})	1.34 x 10E-7 Pa m³/mol (pH 5), 1.60 x 10E-7 Pa m³/mol (pH 7), 1.35 x 10E-7 Pa m³/mol (pH 9) (n.a)
Solubility in water (g/l or mg/l, state temperature)	pH_5:167 g/L at 20°C
	pH 9:165 g/L at 20°C
	pH 7:140 g/L at 20°C (98.1%)
Partition coefficient (log P_{OW}) (state temperature)	pH 5:- 0.8 at 20°C
	pH 9: - 0.9 at 20°C
	pH 7: - 0.8 at 20°C (98.1%)
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH 4: DT50 >250 h at 50 °C
	pH 7: DT50 >250 h at 50 °C
	pH 9: DT50> 250 h at 50 °C
Dissociation constant	10.6 (98.1%) (non-GLP study)
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	
Photostability (DT_{50}) (aqueous, sunlight, state pH)	
Quantum yield of direct phototransformation in water at Σ > 290 nm	

Classification and proposed labelling

with regard to physical/chemical data	
with regard to toxicological data	
with regard to fate and behaviour data	
with regard to ecotoxicological data	

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	
Impurities in technical active substance (principle of method)	

Analytical methods for residues

Soil (principle of method and LOQ)	
Air (principle of method and LOQ)	
Water (principle of method and LOQ)	Reversed phase HPLC-MS/MS. LOQ = 0.025 µg/l
Body fluids and tissues (principle of method and LOQ)	
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	

Chapter 3: Impact on Human Health

Acute toxicity

Rat LD_{50} oral	higher than 2000 mg/kg bw

Repeated dose toxicity

Species/ target / critical effect	Rat, subacute 28-day oral study. Focal/multifocal cortical/medullary mineralization of kidney
Lowest relevant oral NOAEL / LOAEL	It was not possible to determine a LOAEL or a NOAEL for the study with certainty. However, a precautionary approach could be taken in interpreting the results of this study from which a NOAEL of 200 mg/kg/d could be derived, based on agreement in TMI 08.

Genotoxicity	*In vitro* tests (Ames and HPTR): Negative results *In vivo* test (micronucleus test): The conclusion of TM I 08 was that the result is negative.

Other toxicological studies

.....A QSAR analysis: DEREK for Windows, Program version DfW_9.0.0	No structural alerts found

Summary	Value	Study	Safety factor
Non-professional user			
ADI (acceptable daily intake, external long-term reference dose)	not relevant		

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 9: DT_{50} (10°C) = stable DT_{50} (20°C) = stable DT_{50} (25°C) = stable
	pH 7: DT_{50}(10°C)=stable DT_{50}(20°C)=stable DT_{50} (25°C) = stable
	pH 4: DT_{50}(10°C)=stable DT_{50}(20°C)=stable DT_{50} (25°C) = stable
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	
Readily biodegradable (yes/no)	
Biodegradation in seawater	
Non-extractable residues	
Distribution in water / sediment systems	DT50 in water = 967 days (DFOP kinetic model) DT50 in water >1000 days (FOMC-kinetic model) DT90 in water >1000 days (in any kinetic models) DT50 in total system >1000 days (in any kinetic models) DT90 in total system >1000 days (in any kinetic models)
Distribution in water / sediment systems (metabolites)	

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

Mineralization (aerobic)	
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20°C, aerobic, 55% MWHC): geometric mean=153 days (DT50 values in 4 different soils were: 122, 136, 47, 699 days) Geometric mean of 153 days (20°C, 55% MWHC) was used in the risk assessment for calculation of PEC soil. Geometric mean of 127 days (20 °C, normalised to 100% field capacity) was used in the risk assessment for

	calculation of PEC groundwater. ➔the geometric mean DT50 of 127 days (normalized to 100% field capacity) is used in the risk assessment in calculation of N,N-DMS PEC in groundwater. ➔the geometric mean DT50 of 153 days was used in the risk assessment in calculation of PEC soil of N,N-DMS DT_{50lab} (20°C, aerobic):
	DT_{90lab} (20°C, aerobic): DT_{90lab} (20°C, aerobic):
	DT_{50lab} (10°C, aerobic): DT_{50lab} (10°C, aerobic):
	DT_{50lab} (20°C, anaerobic):
	degradation in the saturated zone:
Field studies (state location, range or median with number of measurements)	DT_{50f}:
	DT_{90f}:
Anaerobic degradation	n.a.
Soil photolysis	DT_{50}:
Non-extractable residues	
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	
Soil accumulation and plateau concentration	-

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	No adsorption was detected after 48 hours, therefore determination of Koc and Kd values was not possible, N,N-DMS showed no adsorption to soil in the batch equilibrium experiment. Koc=0 (in the risk assessment of N,N-DMS)

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

Direct photolysis in air	
Quantum yield of direct photolysis	
Photo-oxidative degradation in air	
Volatilization	

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	
Surface water (indicate location and type of study)	
Ground water (indicate location and type of study)	
Air (indicate location and type of study)	

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	Endpoint	Toxicity
Fish			
Rainbow trout (*Oncorhynchus mykiss*)	96 hours	Mortality, LC_{50}	>100 mg/l
	28 days	Reproduction (NOEC)	>100 mg/l
Invertebrates			
Daphnia magna	48 hours	Mortality, LC_{50}	>100 mg/l
	21 days	Reproduction (NOEC)	>100 mg/l
Algae			
Pseudokirchnerella subcapitata	72 hours	Growth inhibition, NOE_rC, E_rC_{50}	> 100 mg/l
Microorganisms			
Activated sludge (mixed population)	3 hours	Oxygen consumption	

Effects on earthworms or other soil non-target organisms

Acute toxicity to …….. (Annex IIIA, point XIII.3.2)	
Reproductive toxicity to …… (Annex IIIA, point XIII.3.2)	Earthworm (*Eisenia fetida*) : (28 days + 28 days) NOEC 361 mg/kg dw Folsomia Candida (28 days): NOEC=316 mg/kg dw, LOEC=1000 mg/kg dw

Effects on soil micro-organisms (Annex IIA, point 7.4)

Nitrogen mineralization	NOEC (28 days) 3.33 mg/kg dw & 17.07 mg/kg dw LOEC >17.07 mg/kg dw
Carbon mineralization	

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	
Acute contact toxicity	

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	
Acute contact toxicity	
Acute toxicity to ……..	

Bioconcentration (Annex IIA, point 7.5)

Bioconcentration factor (BCF)	
Depuration time(DT_{50}) (DT_{90})	
Level of metabolites (%) in organisms accounting for > 10 % of residues	

Chapter 6: Other End Points

Appendix II: List of intended uses

Object and/or situation	Member State or Country	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment			Remarks:
				Type	Conc.	method	number	interval between applications (min)	g as/L	water L/m^2	g as/m^2	
(a)			(c)	(d-f)	of as (i)	kind (f-h)	min max (k)		min max	min max	min max	(m)
Preventive protection against discolourin fungi	**EU**	**Guide Recipe JJT 3580**	**Blue stain fungi**	**Solvent base**	**0 3-0.8 %ww**	***Surface application; brushing, dipping*** **Industrial and professional dipping is normally applied only once, providing protection for many years. For brush applications, dependent on the application amount a 1 to 4 fold application can be required at the beginning. For an application rate of 200 ml product/m^2 a 2 to 3 fold application is necessary. Usual drying time of alkyd based wood preservatives is 12 - 24 hours.**		**min= 0.6 g/m^2** **max = 1.4 g/m^2,** **90 g/m^3**		**Hazard Class 2 only (Above ground, wetting, protected from the weather).**

(a) *e.g.* biting and suckling insects, fungi, molds; (b) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(c) GCPF Codes - GIFAP Technical Monograph No 2, 1989 ISBN 3-8263-3152-4); (d) All abbreviations used must be explained
(e) g/kg or g/l;(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench;
(g) Kind, *e.g.* overall, broadcast, aerial spraying, row, bait, crack and crevice equipment used must be indicated;
(h) Indicate the minimum and maximum number of application possible under practical conditions of use;
(i) Remarks may include: Extent of use/economic importance/restrictions

Appendix III: List of studies

List of studies is a separate document.