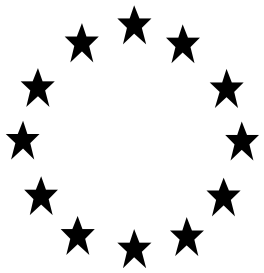
Directive 98/8/EC concerning the placing of biocidal products on the market

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

Assessment Report



Thiabendazole

Product-type 8
(Wood preservatives)

22 February 2008

Annex I - Spain

Thiabendazole (PT 8)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 22 February 2008 in view of its inclusion in Annex I to Directive 98/8/EC

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

This assessment report has been established as a result of the evaluation of Thiabendazole 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.

Thiabendazole (CAS no. 148-79-8) was notified as an existing active substance, by Syngenta European Center, 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.

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

On 11 March 2004, Spain competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 28 June 2004.

On 9 May 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 31 May 2006. The competent authority report included a recommendation for the inclusion of thiabendazole in Annex I to the Directive for PT 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 1 June 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 November 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 and amending Regulation (EC) No 1896/2000. OJ L 307, 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 the basis of the final competent authority report, the Commission proposed the inclusion of thiabendazole in Annex I to Directive 98/8/EC and consulted the Standing Committee on Biocidal Product on 22 February 2008.

In accordance with Article 11(4) of Regulation (EC) No 2032/2003, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 22 February 2008.

1.2. Purpose of the assessment report

This assessment report has been developed and finalised in support of the decision to include thiabendazole 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 thiabendazole. 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 thiabendazole 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

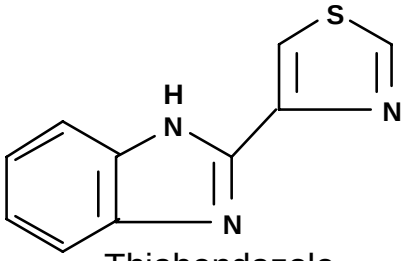
3 http://ec.europa.eu/comm/environment/biocides/index.htm

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

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

CAS-No.	148-79-8
EINECS-No.	205-725-8
CIPAC No.	323
IUPAC Name	2-thiazol-4-yl-1H-benzoimidazole
EC Name	Thiabendazole
CAS Name	1H-Benzimidazole, 2-(4-thiazolyl)-
Common name, synonym	thiabendazole
Molecular formula	C_{10} H_7 N_3 S
Structural formula	 Thiabendazole
Molecular weight (g/mol)	201.26 g/mol
Minimum purity of the active substance as manufactured	985 g / kg

Thiabendazole, technical grade, is a light beige odourless powder at room temperature with a melting point of 297-298 ºC. Its relative density, $D^{20}_{4,}$ is 1.3989 at 20 ºC. Thiabendazole is a solid that thermally decomposes at about 310 ºC. Its vapour pressure is low (4. 6 x 10^{-7} Pa at 25ºC) and hence its Henry's Law Constant indicates that volatilisation is not expected to significantly contribute to the dissipation of thiabendazole in the environment. The solubility in pure water was determined to be 31 mg/l at 25°C (pH 8.1) presenting two dissociation constants. Thiabendazole is not considered highly flammable or explosive or oxidizing. It has no pyrophoric property, does not evolve any flammable gases in contact with water or humid air. Thiabendazole does not ignite below its melting point. Full details of these properties are given in the Annex Listing of End Points at the end of this document.

The methods of analysis of active substance as manufactured and for determination of impurities of toxicological, ecotoxicological or environmental concern or 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, and the methods for analysis in environmental matrices, as appropriate for the assessed uses, have been validated and shown to be sufficiently sensitive with respect to the levels of concern.

2.1.2. Intended Uses and Efficacy

Thiabendazole has been evaluated for its use in wood preservation (main group 02: preservatives, product type 8). The test protocols and the tests results of efficacy are reliable against wood destroying fungi (blue-staining fungi), staining fungi and soft rot fungi.

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against the target organism(s) and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

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

2.1.3. Classification and Labelling

Hazard symbol:	N	Dangerous for the environment
Risk phrases	R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
Safety phrases	S22	Do not breathe dust
	S60	This material and its container must be disposed of as hazardous waste.
	S61	Avoid release to the environment. Refer to special instructions/Safety data sheets.

Justification for the proposal

On the basis of a review of the data submitted, the Spanish Competent Authority suggests that the current classification and labelling of thiabendazole on Annex I to Directive 67/548/EEC is appropriate.

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification and effect assessment

Thiabendazole is a contact and systemic benzimidazole fungicide with protective and curative action. The thiabendazole molecule exerts its fungicidal activity directly and interferes with microtubule assembly by binding to beta tubulin, a protein subunit of microtubules. Microtubules are components of the fungal exoskeleton.

Metabolism

Thiabendazole is rapidly absorbed following oral administration from gastrointestinal tract and is eliminated primarily through the urinary tract. The compound was rapidly distributed to tissues with highest levels found in the heart, lungs, spleen, kidneys, and liver.

In metabolism studies (metabolic transformation by hydroxylation and subsequent conjugation), approximately 75% of the urinary radioactivity was identified chromatographically as either 5-hydroxythiabendazole or its glucuronide or sulphate conjugates. Approximately 60% was identified as the sulphate conjugate with about 15% glucuronide and 1% free 5-hydroxythiabendazole. Trace amounts of 2-acetylbenzimidazole were also recovered in rat urine. The remaining 25% consisted of several unidentified metabolites and trace quantities of 2-acetylbenzimidazole, all present at very low levels. The primary metabolic pathway in rats and a variety of other species studied, including humans, involves oxidation at the 5 position yielding 5-hydroxythiabendazole, followed by conjugation with either glucuronide or sulphate. These metabolites are primarily excreted in urine.

In an additional study, about absorption, metabolism and excretion of thiabendazole in man human volunteers, thiabendazole and its metabolic products were excreted rapidly by the kidney after oral administration of 1 gr of thiabendazole ^{14}C. The rate of elimination was dose-dependent with about 80 to 90% of the total dose eliminated (about 65% urine and 25% faeces) within 24 hours in both sexes treated with 25 mg/kg. At 400 mg/kg the same extent of elimination took about 72 hours, probably due to saturation of metabolic pathways and reduced urine output, important in urinary excretion of thiabendazole.

Dermal absorption

The dermal absorption of thiabendazole has been investigated in an *in vivo* study in the rat following a 6-hours exposure to a concentrated formulation and a 1/50 aqueous dilution, representing 1% thiabendazole, and in two *in vitro* studies in rat and human skin.

In the *in vivo* dermal absorption study, when the formulation was applied as a concentrate for 6 hours, 0.61% of the dose of thiabendazole was absorbed over a 5-day period. When applied as a 1/50 (w/v) aqueous dilution, 3.61% of the applied dose of thiabendazole was absorbed over the same period.

Two studies investigating *in vitro* dermal penetration through rat and human epidermis were conducted. When applied as the in-use 1/50 dilution, 3.75% of the applied dose of thiabendazole penetrated the rat epidermis and 0.16% penetrated the human epidermis over a 6-hour period.

All three studies indicate that the formulation concentrate penetrates significantly less efficient through skin than the 1/50 dilution. For a conservative assessment it is therefore assumed that dermal absorption in humans is equal to or less than 0.15%.

Irritation

For other hand, in irritation and corrosivity studies, the results indicate that thiabendazole is not irritating for eyes and skin.

Skin sensitisation

About sensitisation, the study indicates that thiabendazole is not a dermal sensitizer in guinea pigs. Three guinea pigs died during the study, but these deaths are not believed to be drug related.

Conclusion from repeated dose toxicity studies

Thiabendazole has been studied for its short-term oral toxicity in mice and rat. Only a study about subacute inhalation with a very low reliability has been included, the low toxicity in general of the thiabendazole justified the non-submission of this data. Nevertheless, as it is predicted that thiabendazole would be absorbed by this route it has been considered to predict the consequences of repeated inhalation exposure by extrapolating from repeated oral dosing studies.

Rats: in 28-day study by oral administration in rats the NOEL was < 50 mg/kg b.w/day based on increased thyroid weights and extramedullary hematopoiesis at this dose.

Mice: in 5-weeks study by oral administration the NOEL was 300 mg/kg b.w/day based on body weights and food consumption reductions at 600 mg/kg b.w/day.

Rabbit: there is a 27-day dermal study in rabbit with no toxicologically significant systemic effect observed up to the highest dose used 1000 mg/kg b.w/day. For this reason, the NOEL was > 1000 mg/kg b.w/day.

Subchronic toxicity

In an oral 90-day study in rats a NOAEL of 10 mg/kg b.w/day can be derived based on erythroid hyperplasia in the bone marrow in female rats at doses ≥40mg/kg b.w. Others effects observed at the same dose such as an increased relative liver and thyroid weights with centrilobular and follicular cell hypertrophy, respectively, are rat specific and not relevant to humans, as it is observed in the carcinogenicity and mechanistic studies. The no-observed-effect level in an oral 90-day study in dog was 35 mg/kg b.w/day based on an increased incidence of vacuolation in the gallbladder epithelium at 75 mg/kg b.w/day

Chronic toxicity

In a year study in dog the NOAEL was 10 mg/kg b.w/day based in a gallbladder epithelial vacuolation. Overall, from the oral data, a NOAEL of 10 mg/kg b.w/day is identified from 53-weeks study in dogs based in a cytoplasmatic vacuolation of bile ducts, slight increase in vacuolation of the distal tubules in the kidney and increase hemosiderin and erythropoiesis in the spleen occurring at 40-160 mg/kg b.w/day.

Genotoxicity

Thiabendazole showed no genotoxic potential in *in vitro* tests for induction of point mutations or DNA damage in bacterial and mammalian cells. Moreover, the results of *in vivo* tests were also negative (dominant lethal study and assay for chromosomal aberrations in mouse bone marrow). Therefore, thiabendazole is not classified for mutagenicity.

Carcinogenicity

Thiabendazole did not produce an increased incidence of tumours in mice fed doses as high as 200 mg/kg b.w/day in males and 600 mg/kg b.w/day in females. In rats an increased incidence of benign thyroid adenomas and follicular cell hyperplasia was found at 90 mg/kg b.w/day in females and 30 mg/kg b.w/day in males. This increase in thyroid tumours was associated with increases in liver weight which is well-established to increase thyroxine clearance in rats. This transient decrease in thyroid hormone results in increases in thyroid stimulating hormone (TSH) levels which have a growth promoting effect on the thyroid and increase the incidence of benign thyroid tumours in this species. This mechanism does not occur in humans and, therefore, these findings are not considered relevant for extrapolation to humans. In a study in rats doses ≥ 90 mg/kg b.w/day resulted in significant decreases in thyroid hormone and increases in TSH and thyroid follicular cell hyperplasia which were completely reversible following cessation of treatment. These findings indicate that thiabendazole affects the thyroid in rats indirectly by increasing the clearance of thyroid hormone. NOEL for effects on thyroid hormone and thyroid tumour incidence of 10 mg/kg b.w/day has been established.

Reproductive toxicity

Teratogenicity – developmental study

Thiabendazole has been tested for developmental effects in both rats and rabbits. In these developmental toxicity studies thiabendazole reduced fetal weights only at dose levels that also affected the growth rate in the maternal animals. No developmental anomalies were produced in rats at toxic dose levels. In rabbits a very slight increase in the incidence of hydrocephaly was found at toxic doses in the initial rabbit developmental toxicity study. However, this finding could not be reproduced in a subsequent study in this species. Therefore, thiabendazole is not considered to adversely affect development at non-maternotoxic dose levels in rabbits.

The lowest relevant NOEL was 10 mg/kg b.w/day in rats for maternal and development toxicity, based on decreased body weigh gain and food consumption at doses ≥ 40 mg/kg b.w/day and on decreased pup weight at doses ≥ 40 mg/kg b.w/day respectively.

Fertility – Two reproduction study in rats

Thiabendazole had not effect on reproductive parameters when was tested in 2-Generation Dietary Reproduction Study in rats at concentrations up 90 mg/kg b.w/day; continuous dosing, for 14 consecutive weeks. General effects in parental animals were limited to a decrease in average body weight gain and food consumption in the 30 and 90 mg/kg b.w/day groups and a slight increase in average lactational weight gain in the high dose group. There were no treatment related effects on the survival reproductive performance, or gross lesions at any dose level or histomorphology of reproductive organs at the high dose level. In F2 pups were observed a decreased in average weight in the 90 mg/kg b.w/day group. The NOEL for all

growth survival and reproductive performance parameters observed in this study was 10 mg/kg b.w/day.

Neurotoxicity

The applicant justified that there are no neurotoxicity studies because thiabendazole is not considered a cholinesterase inhibitor or a neurotoxin. The justification is considered acceptable. About mechanistic studies, the applicant presents the following:

A study was carried out to determine if thiabendazole alters thyroxine clearance and affects Thyroid Stimulating Hormone (TSH) or thyroid hormone levels in rats treated for approximately 14 weeks and to determine if the thyroid hyperplasia produced by thiabendazole treatment is reversible. 140 Albino male rats [Crl:CD®(SD)BR strain], were administered thiabendazole by oral feeding to four groups of 35 animals (3 treatment groups and one control group) at dose levels of 10, 90 or 270 mg/kg b.w/day.

In a previously conducted 2-year feeding study with thiabendazole in the rat, thyroid adenomas and thyroid follicular cell hyperplasia were found at dosages ≥ 30 mg/kg b.w/day with a NOEL of 10 mg/kg b.w/day. Therefore this mechanistic study was conducted to determine if the basis of these thyroid changes are related to changes in thyroid hormone homeostasis. The results indicate that thiabendazole affects the thyroid of rats indirectly by altered thyroxine clearance via increased hepatic metabolism. This mechanism is specific to rats and does not result in an increased risk to humans since alterations in thyroid homeostasis do not produce increases in thyroid tumours in humans.

Human cases of acute intoxications

Thiabendazole has been used as a human drug for a number of years and it has been used to have a significant anthelminthic activity against a wide variety of gastrointestinal parasites in animals (nematodes like ascariasis, trichiurasis and trichinosis). The human data have been collected from direct observation in various literature resources.

In one study, observations were conducted in people suffering from trichinellosis in acute and chronic stage and treated in various hospitals. The diagnosis was confirmed by clinical, epidemiologic, serologic findings and in some cases by muscular biopsy. The treatment consisted in the oral or intravenous administration of thiabendazole (500 mg). The number of examined patients totals 31 (21 in acute and 6 in chronic phase of the disease). The results indicate that the parasiticidal effect of thiabendazole alone can not explain its pharmacodynamic action, but thiabendazole is promising as a drug that can be used in people to kill muscular larvae of the parasite.

In other study, the author presents a paper about the results of 232 helminthic infections in 138 patients treated with thiabendazole (25 mg/kg twice a day for two days) in India, and a comparison with 71 helminthic infections in 60 patients treated with other antihelmintics (santonin, tetrachoroethylene, dithiazanine, piperazine with senna or bephenium). The drug was found to have an efficacy and was accepted without any hesitation by all patients and was fairly well tolerated. About 15 per cent of patients receiving the optimum dose of thiabendazole

complained of side effects, the commonest being nausea and vomiting. No toxicity was observed.

In a chronic toxicity study of thiabendazole in 100 male volunteers the results indicate that thiabendazole showed itself to be well tolerated and there were no side reactions or laboratory findings at any time during the study. The study itself was conducted according to a prearranged randomized double-blind design, by which arrangement half of the subjects would receive placebo and half the thiabendazole (125 mg daily) during 6 months.

In an additional study about absorption, metabolism and excretion of thiabendazole in man human volunteers and laboratory animals (dogs and rats), thiabendazole and its metabolic products were excreted rapidly by the kidney after oral administration of 1g of thiabendazole ^{14}C.

Data and safety factors used for deducing AOEL

The calculation of the acceptable operator exposure level (AOEL) is based on the results of the subchronic toxicity and long-term toxicity data, in particular the oral one year study in dog, the 90-day oral toxicity studies in rats and dogs and the subchronic dermal toxicity study in rabbits.

The proposed AOEL should be established on the basis of the dose at which no adverse effects are observed, 10 mg/kg b.w/day for thiabendazole in the 53-weeks oral by capsule in dog, this NOAEL is based on a cytoplasmic vacuolation of bile aducts. In the 90-day dietary rat toxicity study, a NOAEL of 10 mg/kg b.w/day for thiabendazole is established. This NOAEL is based in the erythroid hyperplasia in the bone marrow found at 40 mg/kg b.w/day.

Given the effect observed, the low dermal toxicity, the high degree of oral absorption followed by rapid metabolism and excretion and the long history of safe use of thiabendazole as a fungicide and anthelmintic for animals and humans (up to 50 mg/kg dose taken by humans), a safety factor of 100 is proposed, resulting in an AOEL of 0.1 mg/kg b.w/day.

2.2.1.2. Exposure assessment and risk characterisation

Human health risk for professional users

The application of thiabendazole as wood preservative (PT8) in an industrial and a professional environment can result in direct exposure via skin contact or via inhalation, but the oral ingestion is not considered as a potential direct route for exposure during the use of wood preservatives. As there are not measurements of human exposure, exposure has been estimated with the models provided in the TNsG.

The most relevant exposure path associated to the **industrial procedures** is dermal, and it potentially might happen during the post application task, both in double-vacuum and dipping. Although inhalation is considered to be no significant, it has been assessed considering that used gloves are worn but there is not respiratory protective equipment (RPE).

Regarding the **professional procedures**, the task with potential exposure while in situ spraying is the application of the wood preservative, and the most important route in this case is the inhalation. In the small-scale dipping procedure the inhalation route has been considered as no

relevant and only dermal route of exposure has been assessed for the application task. Finally, the dermal exposure during the application is considered the most relevant for brushing.

Summary of risk assessment for professional operators

Scenario		Systemic NOAEL mg/kg b.w/day	AOEL mg/kg b.w/day	Systemic dose (75%-ile/95%-ile) mg/kg b.w/day	MOE	Exposure/AOEL
Industrial/Professional Double-vacuum (with gloves but without RPE)		10	0.1	0.01204845	830	0.12
				0.0428915	233	0.43
Industrial/Professional *Dipping* (with gloves but without RPE)		10	0.1	0.0291124	343	0.29
				0.104463	96	1.04
Professional In situ spraying (without RPE neither gloves)		10	0.1	0.01825	548	0.18
				0.08515	117	0.85
Professional small-scale dipping (without RPE neither gloves)		10	0.1	0.00147	6803	0.015
				0.001727	5790	0.017
Professional brushing (without protection)	Indoor	10	0.1	0.009248	1081	0.092
				0.018861	530	0.19
	Outdoor	10	0.1	0.003624	2759	0.036
				0.009924	1008	0.099

Workers involved in the professional treatment of wood by spraying or brushing using a solvent-based ready-to-use product containing 1% thiabendazole; the industrial/professional double-vacuum, impregnation technique or the dipping technique using a product containing 50% thiabendazole, are unlikely to be exposed to unacceptable levels of thiabendazole. The MOE calculated are above 100 except for the dipping done by industrial/professional users for a 95%-ile systemic dose where it stays at 96. Nevertheless, this MOE is considered sufficient taking into account that the NOAEL used as basis of MOE calculation was conservative one and the evaluated use is industrial/professional. This default cut-off value of 100 is based on the use of inter and intra-species variability factors, each of 10.

Human health risk for non professional users

Only products containing 1% in ready-to-use mixtures are available to non-professional users. The exposure routes assessed for both brushing and spraying techniques are dermal and

inhalation. While dermal exposure is considered the most relevant for brushing, in the case of spraying the inhalation route is considered to be the most important.

Summary of risk assessment for non-professional operators

Scenario Non-Professional		Systemic NOEL	Systemic AOEL mg/kg b.w/day	Systemic dose mg/kg b.w/day	MOE	Exposure /AOEL
Brushing (without personal protective equipment)	indoor	10	0.1	0.009248	1081	0.092
				0.018861	530	0.19
	outdoor	10	0.1	0.003624	2759	0.036
				0.009924	1008	0.099
Spraying (without personal protective equipment)	indoor	10	0.1	0.025828	387	0.26
				0.034625	289	0.35
	outdoor	10	0.1	0.0033	3030	0.033
				0.006147	1627	0.061

For non-professional users, spraying indoor represents the highest exposure using the product without personal protective equipment and this resulted in a MOE of 289.It is considered that the use of the representative product containing thiabendazole does not show an unacceptable health risk to non-professional users.

Human health risk from indirect exposure as a result of use

Secondary exposure scenarios has been assessed to represent worst cases for all of the relevant exposure routes: dermal (manual handling of wet wood; cleaning work wear at home; children playing on preserved wood), oral (infants chewing preserved timber off-cuts) and inhalation (processing of treated wood).

The handling and processing of treated wood can be performed by professionals as well as by amateurs. The dermal contact while handling wet wood represents the highest exposure. On the other hand, the processing of dry treated wood, especially when it generates large amounts of dust, is considered to be the worst case for exposure by inhalation. Another secondary scenario for adults is the washing of contaminated work clothing and the relevant route for this task is also the dermal mainly to hands.

Children and infants are a group of risk through secondary exposure because they may contact surfaces treated with wood preservatives. When playing on preserved timber, the relevant exposure is dermal; oral exposure might occur when children put their hands into the mouth,

but this is assumed to result in lower exposure than estimated in the scenario of chewing preserved timber off-cuts. This second scenario is then considered to represent the worst case for oral exposure.

Summary of risk assessment for non-users

Secondary exposure Scenario	Calculated exposure		NO(A)EL mg/kg b.w/day	MOE
Intended secondary exposure	Handling of treated wet wood	Prof. and amateurs 0.00497	10	2012
	Processing of treated wood	Professionals 0.00112	10	8929
		Amateurs 0.00014	10	71429
Unintended secondary exposure	Cleaning work wear	(Adult) 0.0023	10	4348
	Playing on preserved timber	Children 0.000015	10	666667
		Infants 0.00003	10	333333
	Chewing preserved timber off-cuts	Double vacuum (infants) 0.04	10	250
		Dipping (infants) 0.015	10	667

The calculated exposure of adults is very low and this results in large MOEs that are considered to be acceptable. Regarding children, estimates of secondary exposure indicated a worst-case systemic dose of 0.04 mg/kg/day for an infant chewing wood treated by double vacuum and 0.00003 mg/kg/day for an infant playing on treated wood play ground structures. For these scenarios, the MOE is above 100 and it is considered to be acceptable.

Human health risk for combined exposure

The potential for combined exposure for the different groups of risk has been calculated adding the indirect exposure to each user. Only the 75^{th} percentile has been considered, because in some scenarios there is no 95^{th} percentile, and always the worst case has been selected.

Summary of risk assessment for combined exposure

User	Total system exposure mg/kg bw/day	NO(A)EL	MOE
Industrial	**0.0622104**	10	**161**
Professional	**0.051348**	10	**195**
Non-Professional	**0.033098**	10	**302**

For an **industrial user**, the estimated worst total systemic exposure, corresponds to dipping technique. If as an amateur, he or she applies thiabendazole by spraying indoor (the worst case among the non-professional techniques) then, it has to be considered the potential secondary exposure as a result of the contact to the residues in air or in surfaces in places where the wood preservative has been used. Finally, the cleaning of work wear is a task that may be carried out by the same person. Adding up all this figures, a MOE of 161 is obtained.

Regarding the **professional user**, the worst case between the application techniques is the in situ spraying. If this user is supposed to fulfil a non-professional application, the handling of treated wood, and the washing of contaminated clothes**,** a MOE of 195 is estimated.

The last scenario for combined exposure is for a **non-professional user**, who applies the product by spraying indoor. Secondarily, this user may be exposed by handling treated wood and cleaning work wear, giving a MOE of 302.

These exposures are considered acceptable.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Fate and behaviour in STP: Thiabendazole is a non biodegradable substance, the greatest percentage (97.5%) of the removal of Thiabendazole resulted in the aquatic phase which discharges to surface waters.

Fate and behaviour in water: Thiabendazole is a compound hydrolytically stable. It is not readily biodegradable in water and is scarcely mineralized to carbon dioxide. The most relevant transformation process within an aqueous environment is the direct phototransformation but the photolytic degradation products, ([^{14}C] Benzimidazole-2-carboxamide and [^{14}C] Benzimidazole) were found in small percents, therefore Thiabendazole parent is the major residue of concern to which non-target species might be exposed.

Fate and behaviour in sediment: Thiabendazole showed a moderate adsorption capacity to sediment. It did not undergo important degradation process and, similarly to the water, the major compound detected in sediments was the parent compound.

Fate and behaviour in air: Thiabendazole is not considered to be a substance of concern for the atmospheric compartment, because it shows slight volatility and a fast atmospheric degradation.

Fate and behaviour in soil: Thiabendazole is photolytically stable in the soil surface, underwent a slow degradation under aerobic and anaerobic conditions in microbially active soils [Benzimidazole, 5-OH-Thiabendazole and $^{14}CO_2$ are the principal degradation products]. Thus, Thiabendazole dissipates slowly (long half-life) and it is essentially immobile in soil and its leaching to groundwater is unlikely.

2.2.2.2. Effects assessment

Effects on aquatic organisms: Thiabendazole may be considered toxic to aquatic organisms. The aquatic PNEC was calculated from the NOEC value for species the most sensitive (*Oncorhinchus mykiss*), based on viability and effects on the development in embryos. The aquatic PNEC was estimated to be 0.0012 mg a.i./L

Effects on sediment organisms: Thiabendazole is not hazardous to sediment organisms. The calculation of the PNEC was based on NOECemmergence for Chironomus. Thus, PNEC for sediment dwelling organisms was estimated to be 0.02 mg a.i./L water or 0.03 mg a.i./kg sediment.

Effects on terrestrial organisms: Thiabendazole does not alter the mineralisation process of carbon and nitrogen in soil, shows a low toxicity to earthworm and collembolla which implies also a low risk to other soil macro-organisms. No adverse effects on ground and foliar dwelling non-target arthropod species are observed. PNEC for soil organisms was estimated from NOEC value to earthworms (based on changes in biomass), being 0.084.

Effects on terrestrial vertebrates (*secondary poisoning*): Thiabendazole shows a low bioconcentration potential in aquatic and terrestrial organisms (BCFfish < 100 and BCFworms < 1) and it does not undergo biomagnification through the food chain. No exposure of wild birds to the formulated product is expected for the specific use applications. Thiabendazole and its formulated product do not represent a real risk to birds due to the low toxicity of the active ingredient. The combination of low avian toxicity and the favourable toxicokinetic profile gave a strong indication that there will not be secondary exposure and that a negligible risk to birds could happen.

2.2.2.3. PBT assessment

Thiabendazole does not fulfil the PBT or vPvB criteria.

2.2.2.4. Exposure assessment

The calculated PEC values for each scenario and environmental compartment are the following:

PEC_{STP}: losses to the STP were calculated for the industrial application stage and for in-service leaching from the wooden commodities according to OECD ESD industrial application and storage scenarios for vacuum pressure, automated spraying (professional and non professional) and dipping, in addition to the scenarios for treated wood in-service for noise barrier which include losses to STP. The greatest emissions of Thiabendazole to STP were observed from industrial applications by vacuum pressure and automated spraying.

PECsw: four emission sources were considered in order to estimate the predicted environmental concentration in surface water: emission via STP, emission by run off and leaching of treated wood in storage and leaching of wood in service-life and direct emission during "in situ" treatments (curative and preventive). It was concluded that the worst proposed scenario for the industrial uses was "vacuum pressure", showing the greatest PECsw -total-value. For the "in situ" application and in-service leaching categories "Brushing bridge outdoor (performed by amateurs)" was the scenario for the life stage of wood-in-service which released the highest amount of Thiabendazole to the aquatic compartment.

PECgw: the information submitted by adsorption/desorption, field dissipation and leaching from soil studies of Thiabendazole suggest that this compound will unlikely leach to deeper soil or groundwater. Potential risk that Thiabendazole would cause in superficial waters through its leaching from soil to groundwaters is covered by the estimated risk for superficial waters.

PEC in sediment: Thiabendazole has a short half-life in water migrating to the sediment within a short time period. The concentration in sediment was derived from the corresponding water body concentration, assuming equilibrium partitioning. The greatest PEC in sediments were observed from dipping industrial application scenario and from brushing bridge outdoor (performed by amateurs) in service scenario according to the results obtained in superficial waters.

PEC in air: PEC in air only should be calculated for industrial preventive treatment. Taking into account the low volatility of Thiabendazole, its emission to the atmosphere during treatment application is not considered relevant. Therefore, it is not meaningful to predict the PEC in air.

PEC in industrial soil and in soil where commodities of treated wood are placed: terrestrial compartment can be exposed to Thiabendazole via: leaching of treated wood (by vacuum pressure, automated spraying and dipping) in storage, leaching of in service wood (noise barrier, fence and house), emissions from "in situ" applications (noise barrier, fence and house), leaching subsequent to "in situ" applications (by brushing). The scenarios that contributed with the greatest emissions of Thiabendazole to the soil were: industrial application treatments of "double vacuum" and "dipping", "house scenario" for treated wood-in-service and "brushing house outdoor (performed by amateurs)" for in-situ treatments.

PEC in agricultural and grassland soils: emissions of Thiabendazole to agricultural and grassland soils after application of sludge from sewage treatment plant were negligible compared with those from treated wood in industrial storage and wood commodities in service. It was likely because the fraction of emission directed to sludge by STP is very low (2.5%).

Non compartment specific exposure relevant to the food chain (secondary poisoning): neither accumulation of Thiabendazole in tissues of fish and earthworms or biomagnification through food chain has been evidenced for Thiabendazole. Therefore it was not considered necessary to calculate a PEC for food chain risk assessment.

2.2.2.5. Risk characterisation

Results of the risk assessment for Thiabendazole in the different environmental compartments are shown below.

Sewage treatment plant organisms: acceptable risk to sewage treatment plant organisms from industrial applications and in-service leaching from noise barriers was found.

Aquatic organisms: unacceptable risk for wildlife (fish, aquatic invertebrates and algae) of aquatic environment was identified for industrial treatments from the intended use of the product and its active ingredient Thiabendazole as wood preservative since the calculated PEC/PNEC ratio was higher than 1. Only the noise barrier, as in-service scenario, shows acceptable risk for aquatic organisms. The curative or preventive wood treatments performed in situ by “brushing” represent the highest potential risk for aquatic compartment.

Sediment organisms: unacceptable risk for sediment was identified for industrial treatments from the intended use of the product and its active ingredient Thiabendazole as wood preservative since the calculated PEC/PNEC ratio was higher than 1. The noise barrier, as in-service scenario, also shows unacceptable risk for sediment dwelling organisms. The curative or preventive wood treatments performed in situ by “brushing” represent the highest potential risk for sediment compartment.

Atmosphere: contamination of the air with Thiabendazole should not be expected due to its low volatility. Thiabendazole shows a very fast atmospheric degradation. This type of emission was not considered relevant. Thereby, the risk assessment for the atmosphere was not calculated.

Terrestrial organisms: there is very high risk to produce adverse effects in terrestrial organisms when they were exposed to the product and its active ingredient Thiabendazole as wood preservative according to indicated practices and to label recommendations.

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. DECISION

3.1. Background to the Decision

The overall conclusion from the human health evaluation of thiabendazole for use in product type 8 (wood preservatives) is that the assessment of biocidal products containing no more than of 1% w/w of thiabendazole shows no unacceptable risk to humans under the proposed conditions of use. This conclusion relies on the fact that industrial/professional uses will be applying the basic principles of good practice and using appropriate and obligatory PPE, in particular for the dipping process.

The assessment for non-professional users shows no unacceptable health risk when it is used by brushing and spraying, both indoor and outdoor.

The assessment of secondary exposure shows that adult, children and infants will not be exposed to unacceptable levels of thiabendazole during the realistic worst-case scenarios presented.

The environmental risk assessment indicates that thiabendazole in industrial and in service (use hazard class 3) scenarios currently shows an unacceptable risk for the aquatic and terrestrial compartments. Uses in hazard class 1 and 2 (situation in which wood or wood-based product is under cover) show no unacceptable risk provided certain risk mitigation measures are applied.

3.2. Decision regarding Inclusion in Annex I

The thiabendazole 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:

(1) The active substance thiabendazole, as manufactured, shall have a minimum purity of 985 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 and/or professional use, with respect to the double-vacuum and dipping application tasks, must be used with appropriate personal protective equipment, unless it can be demonstrated in the application for product authorisation that risks to workers and operators can be reduced to an acceptable level.

(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
(a) freshly treated timber must be stored after treatment on impermeable hard standing to prevent direct losses to soil and that any losses must be collected for reuse or disposal; and
(b) application solutions must be collected and reused or disposed of as hazardous waste and that wastewater from application plant must not be released directly to surface water or any kind of sewer unless it can be demonstrated in the application for product authorisation that risks to aquatic compartment can be reduced to an acceptable level.

In addition, products cannot be authorised for the treatment of wood that will be used outdoors unless data is submitted to demonstrate that the product will meet the requirements of Article 5 and Annex VI, if necessary by the application of appropriate risk mitigation measures.

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

- Products containing thiabendazole may be used in the pre-treatment of wood by double-vacuum process and dipping by industrial users, small scale dipping, *in situ* spraying and brushing by professional users and finally brushing and spraying by non-professional users.
- Thiabendazole has shown some efficacy against wood destroying fungi, staining fungi and soft rot fungi. However, further efficacy data will be required to support product authorisation at the Member State level.

If a sufficient efficacy of Thiabendazole can only be reached by increasing the application rate, new PEC/PNEC ratios should be calculated. In this case, the applicant should provide the new application rates.

- Products containing thiabendazole may only be used for wood class 1 and 2 establishing one effective depuration system in the sewage treatment plant to reduce the levels of thiabendazole in wastewater or containing, recycling and treating as waste losses during industrial application as well as during tank cleaning, in accordance with the national regulations of the Member State authorising individual products, together with storing treated timbers on hard standing to prevent direct losses to soil in industrial areas of storage.

The results of the risk evaluation of biocidal products containing thiabendazole as wood preservative could be reconsidered for hazard class 3 if the applicant provides:

- a proposal of one depuration system to reduce the high concentrations of Thiabendazole in the wastewater to the required level to guarantee an acceptable risk for the aquatic ecosystem of the receiving waters including sediment dwelling organisms

or/and

- additional studies in aquatic organisms to apply a probabilistic method in the estimation of the PNEC aquatic value or studies in mesocosms together with sediment-water Chironomid toxicity test using spiked sediment (OECD guideline 218) and a test on *Lumbriculus variegatus* as specified in the Technical Guidance Document on Risk Assessment, part II (App VI, Table 1, pp.298).

and

-additional studies in terrestrial organisms to refine the probabilistic method used to estimate of the PNECs value.

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 thiabendazole in Annex I to Directive 98/8/EC.

3.5. Updating this Assessment Report

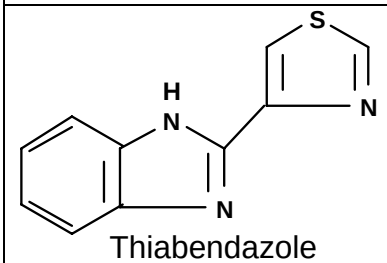
This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information referred to in Articles 7, 10.4 and 14 of Directive 98/8/EC. Such adaptations will be examined and finalised in connection with any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

Appendix I: List of endpoints

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

Active substance (ISO Common Name)	Thiabendazole
Product-type	Fungicide

Identity

Chemical name (IUPAC)	2-thiazol-4-yl-1H-benzoimidazole
Chemical name (CA)	1H-Benzimidazole, 2-(4-thiazolyl)-
CAS No	Thiabendazole
EC No	148-79-8
Other substance No.	205-725-8
Minimum purity of the active substance as manufactured (g/kg or g/l)	985 g / kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None of relevance
Molecular formula	$C_{10}H_7N_3S$
Molecular mass	201.26
Structural formula	 Thiabendazole

Physical and chemical properties

Melting point (state purity)	297 - 298 °C
Boiling point (state purity)	Thermal decomposition before the boiling point is reached
Temperature of decomposition	310 ºC
Appearance (state purity)	Off-white to yellow tan coloured powder
Relative density (state purity)	D_4^{20} 1.3989
Surface tension	σ = 72.7 mN/m (90 % saturation concentration) at 20 ºC
Vapour pressure (in Pa, state temperature)	$4.6 \cdot 10^{-7}$ Pa at 25ºC
Henry's law constant (Pa m^3 mol^{-1})	$1.4 \cdot 10^{-6}$ Pa m^3 mol^{-1}
Solubility in water (g/l or mg/l, state temperature)	0.16 g/l at pH 4 (20 ºC) 0.03 g/l at pH 7 (20 ºC) 0.03 g/l at pH 10 (20 ºC) 0.031 g/l at pH 8.1 (25 ºC)
Solubility in organic solvents (in g/l or mg/l, state temperature)	at 20 ± 0.5°C g/l n-heptane: <0.01 xylene: 0.13 methanol: 8.28 1,2-dichloroethane: 0.8 acetone: 2.43 ethyl acetate: 1.49 n-octanol: 3.91
Stability in organic solvents used in biocidal products including relevant breakdown products	Thiabendazole is stable in organic solvents. Nevertheless, the biocidal product is not formulated in organic solvents
Partition coefficient (log P_{OW}) (state temperature)	pH 4: $\log_{10} K_{ow}$: 1.62 ± 0.01 (at 20 ± 0.5 °C) pH 7: $\log_{10} K_{ow}$: 2.39 ± 0.14 (at 20 ± 0.5 °C) pH 10: $\log_{10} K_{ow}$: 2.40 ± 0.04 (at 20 ± 0.5 °C)
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	pH 5: DT_{50}: 357 days (at 25°C); DT_{50} (12 ºC) = 999 pH 7: DT_{50}: 203 days (at 25°C); DT_{50} (12 ºC) = 586 pH 9: DT_{50}: 271 days (at 25°C); DT_{50} (12 ºC) = 758
Dissociation constant	pKa: 4.73 and 12.00
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	UV absorption maxima at 254 nm and 302 nm
Photostability (DT_{50}) (aqueous, sunlight, state pH)	DT_{50}: 29 hours at pH 5 and 25°C
Quantum yield of direct phototransformation in water at Σ > 290 nm	Not applicable.

Flammability and autoflammability	Combustion time > 4 minutes (6 min 48 sec) and therefore not considered as highly flammable. Thiabendazole does not spontaneously ignite on contact with air at ambient temperatures. It is not classified as highly flammable in terms of its pyrophoric properties.
Explosive properties	None. Does not generate heat in the presence of oxygen or undergo exothermic decomposition.
Oxidizing properties	The test substance has no oxidizing properties

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	N , R50/53, S61

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	The determination of the active substance, thiabendazole, was carried out with liquid chromatography on a Nucleosil C18 column using 0.1 M aqueous ammonium acetate as eluent with a linear gradient program and UV detection at 254 nm. Quantification by comparison of peak area with an external standard.
Impurities in technical active substance (principle of method)	As above

Analytical methods for residues

Soil (principle of method and LOQ)	Residues of thiabendazole (and, where appropriate, its benzimidazole metabolite) are determined high pressure liquid chromatography (HPLC) using fluorescence detection using thiabendazole analytical standard (99.8% pure). LOQ of the analytical method in soil is 0.01 mg/kg
Air (principle of method and LOQ)	Analytical method for thiabendazole in air is not required as its vapour pressure does not exceed the trigger value of 1×10^{-5} h Pa (mm Hg).
Water (principle of method and LOQ)	Residues of thiabendazole are determined spectrofluorometrically after liquid partitioning LOQ is 0.05 µg/kg
Body fluids and tissues (principle of method and LOQ)	Residues of thiabendazole and its metabolite in human serum were determined high pressure liquid chromatography (HPLC) using fluorescence detection. LOD for thiabendazole is 0.1 mg/l
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Residues of thiabendazole (and, where appropriate, its benzimidazole metabolite) are determined high pressure liquid chromatography (HPLC) using fluorescence detection.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Residues of thiabendazole (and, where appropriate, its benzimidazole metabolite) are determined high pressure liquid chromatography (HPLC) using fluorescence detection.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	At least 67 % - 75 % based on urinary excretion within 168 h
Rate and extent of dermal absorption:	• In the *in vivo* dermal absorption study, when the product was applied as a concentrate for 6 hours, 0.61% of the dose of thiabendazole was absorbed over a 5-day period. When applied as a 1/50 aqueous dilution, 3.61 % of the applied dose of thiabendazole was absorbed over the same period. • Two studies investigating *in vitro* dermal penetration through rat and human epidermis were conducted in parallel with the *in vivo* study. When applied as the in-use a 1/50 dilution , 3.75% of the applied dose of thiabendazole penetrated the rat epidermis and 0.16% penetrated the human epidermis over a 6-hour period. When the product was applied as a concentrate, the percentage of thiabendazole was below the limit of detection (<0.04%) for both the rat and the human epidermis. According to these data, the dermal absorption estimated for humans is 0.15%.
Distribution:	Widely.
Potential for accumulation:	Low.
Rate and extent of excretion:	85 % - 92 % within 24 h, mainly via urine
Toxicologically significant metabolite(s)	5-hydroxythiabendazole

Acute toxicity

Rat LD_{50} oral	Male: LD_{50} oral: 5070 mg/kg Female: LD_{50} oral: 4734 mg/kg
Rat LD_{50} dermal	> 2000 mg/kg bw
Rat LC_{50} inhalation	> 6.84 mg/l (maximum concentration achieved)
Skin irritation	No irritation
Eye irritation	No irritation
Skin sensitization (test method used and result)	No sensitisation (Maximisation test)

Repeated dose toxicity

Species/ target / critical effect	Cytoplasmic vacuolation of bile aducts (dog) and erythroid hyperplasia in the bone marrow (rat)
Lowest relevant oral NOAEL / LOAEL	NOAEL= 10 mg/kg bw/day (53 weeks, dog) NOAEL= 10 mg/kg bw/day (90 d, rat)
Lowest relevant dermal NOAEL / LOAEL	> 1000 mg/kg bw/d (23 d, rabbit)
Lowest relevant inhalation NOAEL / LOAEL	Not established.

Genotoxicity	Thiabendazole showed no genotoxic potential in *in vitro* and *in vivo*
Carcinogenicity	
Species/type of tumour	Thyroid adenomas and follicular cell hyperplasia due to liver enzyme induction in rats (based on the available data).
lowest dose with tumours	10 mg/kg bw /d (2 year study, rat) NOEL
Reproductive toxicity	
Species/ Reproduction target / critical effect	No reproductive toxic effects at parental toxic doses in rats / decrease body weight and food consumption
Lowest relevant reproductive NOAEL / LOAEL	> 90 mg/kg bw/d for reproduction 10 mg/kg bw/d for parents and offspring
Species/Developmental target / critical effect	Not teratogenic. Fetotoxic at maternal toxic dose
Developmental toxicity	
Lowest relevant developmental NOAEL / LOAEL	No reproductive toxic effects at parental toxic doses in rats / decrease body weight and food consumption
Neurotoxicity / Delayed neurotoxicity	
Species/ target/critical effect	No studies have been submitted and waiving was accepted. No indication of neurotoxicity in standard short and long term toxicity studies
Lowest relevant developmental NOAEL / LOAEL.	-
Other toxicological studies	
.....	Mechanistic studies indicate effects on thyroid hormones due to liver enzyme induction in rats
Medical data	
.....	A NOAEL of 3 - 4 mg/kg bw /d was proposed by WHO for human beings Adverse reactions have been reported at therapeutic dose of 50 mg/kg bw/d over 2 d

Summary	Value	Study	Safety factor
Non-professional user			

ADI (acceptable daily intake, external long-term reference dose)	Not applicable		
AOEL-S (Operator Exposure) Medium and chronic	0.1 mg/kg bw/d	One year study in dog and the 90 day oral toxicity in rats	100
ARfD (acute reference dose)	Not required		

Acceptable exposure scenarios (including method of calculation)

Professional users	The industrial and a professional application of thiabendazole as wood preservative (PT8) can result in direct exposure via skin contact or via inhalation, but the oral ingestion is not considered as a potential direct route for exposure. As there are not measurements of human exposure, exposure has been estimated with the models provided in the TNsG. The most relevant exposure path associated to the **industrial procedures** is dermal, and it potentially might happen during the post application task, both in double-vacuum and dipping. The exposure has been estimated with **Handling model** 1 of the TNsG. Although inhalation is considered to be no significant, it has been assessed as well, and the estimated total exposure, considering that used gloves are worn but there is not respiratory protection. Regarding the **professional procedures**, the task with potential exposure while in situ spraying (**Spraying model 2**) is the application of the wood preservative, and the most important route in this case is the inhalation. In the small-scale dipping application (**Dipping model 1**) the inhalation route has been considered as no relevant and only dermal route of exposure has been assessed for the application task. Finally, the dermal exposure during the application is considered the most relevant for brushing (**Consumer product painting, indoor model 1 and outdoor, model 3).**
Non-professional users	Only product containing 1% in ready-to-use formulations are available to non-professional users, therefore mixing and loading is no a relevant task for this group. The total systemic exposure has been estimated for the application of the wood preservative and the cleaning of the equipment without personal protective equipment, and the exposure routes assessed for both brushing (**Consumer product painting, indoor model 1 and outdoor, model 3**)and spraying techniques (**Consumer product spraying & dusting, model 3**), are dermal and inhalation. While dermal exposure is considered the most relevant for brushing, in the case of spraying the inhalation route is considered to be the most important.

Indirect exposure as a result of use	Secondary exposure scenarios have been assessed to represent worst cases for all of the relevant exposure routes: dermal (manual handling of wet wood; cleaning work wear at home; children playing on preserved wood), oral (infants chewing preserved timber off-cuts) and inhalation (processing of treated wood). The handling and processing of treated wood can be performed by professionals as well as by amateurs, and dermal contact while handling wet wood represents the highest exposure. On the other hand, the processing of dry treated wood is considered to be the worst case for exposure by inhalation. Another secondary scenario for adults is the washing of contaminated work clothing and the relevant route for this task is also the dermal mainly to hands. Children and infants are a group of risk through secondary exposure by contact with surfaces treated with wood preservatives. When playing on preserved timber, the relevant exposure is dermal; oral exposure might occur when children chew preserved timber off-cuts and this scenario is considered to represent the worst case for oral exposure.

Chapter 4- 4.1.: Fate and Behaviour in the Environment

Active substance:

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 5: DT_{50} (25 ºC) = 357; DT_{50} (12 ºC) = 999 (stable)
	pH 7: DT_{50} (25 ºC) = 203; DT_{50} (12 ºC) = 586 (stable)
	pH 9: DT_{50} (25 ºC) = 271; DT_{50} (12 ºC) = 758 (stable)
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	DT_{50}: 29 hours at pH 5 and 25 ºC. Several minor metabolites as Benzimidazole < 10 %; and one metabolite at 10.22 % at one timepoint (Benzimidazole-2-carboxamide).
Readily biodegradable (yes/no)	No.
Biodegradation in seawater	-
Non-extractable residues	Non-extractables accounting for at maximun ca 32 to ca 65 %
Distribution in water / sediment systems (active substance)	$DT_{50\ water}$ (20 ºC): 1.6 and 2.3 days (river/pond) $DT_{90\ water}$: 5.3-7.8 days (river/pond) $DT_{50\ total\ system}$: 4.3 and 4.4 days (river/pond) (1st comp.) 4332 and 375 days (river/pond) (2nd comp.) $DT_{50\ total\ system}$: 2406 and 5.4 days (river/pond) $DT_{90\ total\ system}$: 12465 and 825 days (river/pond) DT_{50} (12 ºC)= $2406*e^{(0\ 08*(20-12))}$ = 4571.40 days (river) DT_{50} (12 ºC)= $5.4*e^{(0\ 08*(20-12))}$ = 10.26 days (pond) Water: 94 % at day 0 to < 10 % at day 14 Sediment: 20-40 % at day 1 to 30-71 % at day 181 Rapid binding of the a.s. to the organic matter of suspended particles and sediments.
Distribution in water / sediment systems (metabolites)	Water and sediment with degradates < 2 % at all time points Mineralization: 0.5-1.8 % at day 180 Non-extractables accounting for at maximun ca 32 to ca 65 %

Route and rate of degradation in soil

Mineralization (aerobic)	5.59 % after 365 days
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (25°C, aerobic): > 730 days $DT_{50\ lab}$ (12°C, aerobic, sandy loam soil): 2044 days DT_{50lab} (20°C, aerobic, silt loam soil): 33 days $DT_{50\ lab}$ (12°C, aerobic, silt loam soil): 62.7 days DT_{50lab} (25°C, aerobic, sandy loam soil): 211 days $DT_{50\ lab}$ (12°C, aerobic, sandy loam soil): 590.8 days
	DT_{90lab} (20°C, aerobic): not calculated
	DT_{50lab} (10°C, aerobic): not calculated
	DT_{50lab} (20°C, anaerobic): not calculated
	degradation in the saturated zone: not calculated
Field studies: soil accumulation studies	DT_{50f}: 1093-1444 days
	DT_{90f}: not calculated
Anaerobic degradation	Stable to anaerobic degradation
Soil photolysis	DT_{50f}: 933 days ; photolytically stable
Non-extractable residues	12.50 % after 365 days
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	None
Soil accumulation and plateau concentration	-

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	$K_{OC,ads}/K_{OC,des}$ = 1812/1336 silt loam 3992/4865 sandy loam 1104/3260 sand 22467/18325 clay* 21.8 (silt loam, pH 7.1), 16 (sandy loam, pH 6.5), 2.8 (sand, pH 7.4), 270 (clay, pH 6.7) * (extreme case due to a clay content of 58%, this was not used in the risk assessment)

Mobility

Laboratory studies :

Column leaching :	Immobile
Aged residue leaching:	Immobile > 98 % remained in the top 2.5 cm layer

Field studies:

Lysimeter/Field leaching studies :	No data

Fate and behaviour in air

Direct photolysis in air	Not relevant
Quantum yield of direct photolysis	Not relevant
Photo-oxidative degradation in air	Estimation acc. to Atkinson calculation: DT_{50} = 2-3.5 hours
Volatilization	slightly volatile

Chapter 4- 4.2.: Ecotoxicology

Aquatic Organisms

Species	Time-scale	Endpoint
Fish		
Salmo gairdneri	96 h, flow-thr.	LC_{50} = 0.55 mg/L
Cyprinodon variegatus	96 h, flow-thr.	LC_{50} > 10 mg/L
Salmo gairdneri	30 d, flow-thr.	NOEC = 0.012 mg/L embryo/larvae
Invertebrates		
Daphnia magna	48 h, flow-thr.	EC_{50} = 0.81 mg/L
Mysidopsis bahia	96 h, flow-thr.	EC_{50} (48 h)=0.74 mg/L
Daphnia magna	21 d, flow-thr.	NOEC = 0.042 mg/L survival/reproduction
Chironomus riparius	23 d	NOEC > 2.0 mg/L or NOEC > 3.0 mg/kg sediment emergence/development
Algae		
Selenastrum capricornutum	96 h	IC_{50} = 8.99 mg/L NOEC <1 mg/L growth

Bioconcentration

Bioconcentration factor (BCF)	Species: *Lepomis macrochirus* Time-scale: 28 d (exposure phase) 14 d (depuration phase) Test system: flow-thr. Endpoint: BCF (whole fish)= 96.45 BCF (edible portion)= 22.84 BCF (visceral tissue)= 642.00
Depuration time(DT_{50}) (DT_{90})	DT_{90}=14 days
Level of metabolites (%) in organisms accounting for > 10 % of residues	Edible tissue: 32% was identified as 5-hydroxy-Thiabendazole Visceral tissues:50% associated with 5-hydroxy-Thiabendazole

Target organisms

Growth inhibition to fungi	Time-scale: 3-14 d *Marasmius oreades, Paecilomyces marquandii, Mucor circinelloides*:

	NOEC (growth inhibition):18.1 mg a.i./kg soil Phytophtera nicotianae: NOEC (growth inhibition) > 54.3 mg a.i./kg soil
Soil micro-organisms	
Nitrogen mineralization	No effects up to 9 mg/kg soil
Carbon mineralization	No effects up to 9 mg/kg soil
Earthworms	
Reproductive and growth toxicity to *Eisenia fetida*	Time-scale: 56 d NOEC (based on survival, reproduction and biomass) ≥ 4.2 mg a.i./kg soil
Terrestrial plants	
Lactuca sativa, *Raphanus sativus* and *Triticum aestivum*	Time-scale: 18 d EC_{50} (*Lactuca sativa*) = 4.65 mg ai/kg EC_{50} (*Raphanus sativus*) = 5.18 mg ai/kg EC_{50} (*Triticum aestivum*)= 7.83 mg ai/kg
Effects on honeybees	
Acute oral toxicity	Time-scale: 48 h LD_{50} > 4µg/bee
Acute contact toxicity	Time-scale: 48 h LD_{50} > 34µg/bee
Other arthropod species	
Reproductive toxicity to *Folsomia candida*	Time-scale: 28 d NOEC (survival/reproduction) = 10 mg a.i./kg soil
Terrestrial vertebrates	
Acute toxicity to birds	Time-scale: Dosing with a single oral dose and observation during 14 d (post-dosing) Quail LD_{50} > 2250 mg/Kg bw
Dietary toxicity to birds	Time-scale: 5 d Duck LC_{50} > 5946 mg/kg diet
Reproductive toxicity to birds	Time-scale: 119 d Quail NOEC ≥ 400 mg/kg diet

STP microorganisms

Microorganisms			
Activated sludge from the waste-water treatment plant (bacteria community)	3 h	EC_{50} > 1000 mg ai/L NOEC = 31 mg ai/L (water solubility)	-

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	Endpoint
Fish		
Salmo gairdneri	96 h, static conditions.	LC_{50} = 2.2 mg/L (0.99 mg a.i./L)
Invertebrates		
Daphnia magna	48 h, flow-thr.	EC_{50} (48 h)= 1.4 mg/L (0.63 mg a.i./L)

Earthworms

Acute toxicity to … *Allolobophora spp.*; *Lumbricus terrestris* and other species	Time-scale: 14 d. LC_{50} = 31.9 mg/kg soil (19.1 mg a.i./kg soil)
	Time-scale: 14 d. LC_{50} > 1000 mg/kg soil (> 449 mg a.i./kg soil)
Reproductive toxicity to *Eisenia foetida*	Time-scale: 56 d. NOEC (change in biomass/number of offspring) <4.5 mg a.i./ha (13.91 mg ai/kg soil)

Bioconcentration

Bioconcentration factor (BCF)	Species: *Eisenia foetida* Time-scale: 28 d (exposure phase) 28 d (depuration phase) Endpoint: BCF = 0.1
Depuration time(DT_{50}) (DT_{90})	DT_{90}=28 days

Arthropods species

Test species	
Aphidius rhopalosiphi	Effect % (0.12, 0.06, 0.0042 kg a.i./ha) Time-scale: 48 h Mortality: 3 %

	Fecundity: reduction on reproduction 55 % (0.12 kg a.i./ha)
Aleochara bilineata	Effect % (1x = 0.9 Kg/ai/ha; 2x = 1.8 Kg/ai/ha) Time-scale: 70 d Mortality: No effect Fecundity: reduced by 27% (1x and 2x)
Chrysoperla carnea	Effect % (1x = 0.9 Kg/ai/ha; 2x = 1.8 Kg/ai/ha) Time-scale: 46 d Mortality: 16 % and 4 % (1x, 2x) for larvae and pupae Fecundity: 27 %
Typhlodromus pyri	Effect % (1x = 0.9 Kg/ai/ha; 2x = 1.8 Kg/ai/ha) Time-scale: 14 d. Mortality: 3 % Fecundity: reduction on reproduction 5 % (2x)

Chapter 6: Other End Points

Not applicable

Appendix II: List of Intended Uses

The foreseen intended uses of thiabendazole are:

- industrial wood preservation. The application techniques are double-vacuum process and dipping.

- *in situ* remedial wood preservation by professionals. These are mainly small scale dipping, spraying and brushing using ready to use mixed formulations (1% thiabendazole)

- do-it-yourself treatment of wood (non-professional). The application techniques are brushing and spraying, both indoor and outdoor. Using ready to use mixed formulations (1% thiabendazole)

Products containing Thiabendazole may only be used for wood class 1 and 2 establishing one effective depuration system in the sewage treatment plant to reduce the levels of Thiabendazole in wastewater or containing, recycling and treating as waste losses during industrial application as well as during tank cleaning, in accordance with the national regulations of the Member State authorising individual products, together with storing treated timbers on hard standing to prevent direct losses to soil in industrial areas of storage.

Appendix III: List of studies

Data protection is claimed by the applicant in accordance with Article 12.1(c) (i) and (ii) of Council Directive 98/8/EC for all study reports marked "Y" in the "Data Protection Claimed" column of the table below. For studies marked Yes(i) data protection is claimed under Article 12.1(c) (i), for studies marked Yes(ii) data protection is claimed under Article 12.1(c) (ii). These claims are based on information from the applicant. It is assumed that the relevant studies are not already protected in any other Member State of the European Union under existing national rules relating to biocidal products. It was however not possible to confirm the accuracy of this information.

Annex point / reference number Doc IIIA	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner (1)
2.2 2.5.2	Burkhard, N.	1997	Structure and Nomenclature Novartis Crop Protection AG, Basel, Switzerland 21.08.1997 Syngenta File N° MK360/0150	Y	SYN
3.0	Stulz, J.	2001	Physico-Chemical Properties Syngenta Crop Protection AG, Basel, Switzerland 09.08.2001 Syngenta File N° MK360/0456	Y	SYN
3.1.1	Boos, R.N.	1973	Determination of sublimation pressure, heat of sublimation and loss of weight at 25°C and 49°C Merck Sharp & Dohme Ltd., Hoddesdon, United Kingdom 5734 0360, 22.01.1973 Syngenta File N° MK360/0128	Y	SYN
3.1.1 3.1.3 3.5 3.7 3.11	Pigeon, O.	1997	Physical and chemical properties of thiabendazole technical (5 batch analysis, melting point, density, water solubility, solubility in organic solvents, log Pow, flammability) Station de phytopharmacie, Gembloux, Belgium 09.07.1997 Syngenta File N° MK360/0169	Y	SYN
3.1.2	Das, R.	2000	Boiling point / boiling range of MK 360 Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland 85208, 08.08.2000 Syngenta File N° MK360/0568	Y	SYN
3.2	Widmer, H.	1999	Vapour pressure of MK 360 Novartis Crop Protection AG, Basel, Switzerland 99WI27, 15.11.1999 Syngenta File N° MK360/0552	Y	SYN
3.2.1	Burkhard, N.	2000	Henry's law constant Novartis Crop Protection AG, Basel, Switzerland 11.05.2000 Syngenta File N° MK360/0533	Y	SYN
3.3	Das, R	2005	MK 360 Color, Physical state, odor Syngenta Crop Protection Münchwilen AG, Münchwilen, Switzerland 113737, 13.01.2005		
3.4	Oggenfuss, P.	1999	Spectra of MK 360 Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland 77466, 23.09.1999 Syngenta File N° MK360/0547	Y	SYN
3.5	Das, R.	2001	Water solubility of MK 360 (pure water) Syngenta Crop Protection Münchwilen AG, Münchwilen, Switzerland 107827, 30.07.2001 Syngenta File N° MK360/0580	Y	SYN
3.6	Book, D.E. Thomas, E.A.	1988	Thiabendazole - Product Chemistry (Determination of dissociation constant)	Y	SYN

Annex point / reference number Doc IIIA	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner (1)
			Ricerca, LLC, Concord, United States 15.11.1988 Syngenta File N° MK360/0130		
3.10	Düll, B.	2002	Shelf-life statement for thiabendazole (LOT 9719713294) Syngenta Crop Protection Münchwilen AG, Münchwilen, Switzerland 30.09.2002 Syngenta File N° MK360/0607	Y	SYN
3.10	Angly, H.	1999	Screening test for thermal stability and stability in air Institute of Safety and Security, Basel, Switzerland 1999.4034.TSA, 17.05.1999 Syngenta File N° MK360/0532	Y	SYN
3.11	Jackson, W.A.	2007	MK360 - Flammability (Pyrophoric Properties) Syngenta Crop Protection Münchwilen AG, Münchwilen, Switzerland HT07/014, 16.03.2007	Y	SYN
3.11	Jackson, W.A.	2007	MK360 - Relative Self-Ignition Temperature for Solids Syngenta Crop Protection Münchwilen AG, Münchwilen, Switzerland HT07/015, 16.03.2007	Y	SYN
3.13	Martin, N.	2000	Surface tension Solvias AG, Basel, Switzerland PP-00/28C.SUR, 10.07.2000 Syngenta File N° MK360/0569	Y	SYN
3.15	Welberry, R.J.	1988	Thiabendazole : Explosivity tests of 2,-(4-tiazolyl) benzimidazole Hercules Inc., Rocket Center, WV, United States 01.08.1988 Syngenta File N° MK360/0131	Y	SYN
3.16	Jackson, W.A.	2002	Oxidising properties – MK 360 microfine Syngenta Technology & Projects, Huddersfield, United Kingdom HT02/109, 04.02.2002 Syngenta File N° MK360/0590	Y	SYN
3.17	Kundel, P.	2002	Corrosion characteristics (microfine) Syngenta Crop Protection Münchwilen AG, Münchwilen, Switzerland 108604, 18.04.2002 Syngenta File N° MK360/0591	Y	SYN
4.1	Düll, B.	1998	Analytical Method – Thiabendazol – Content by HPLC chromatography Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland AW-207/1, 23.07.1998 Syngenta File N° MK360/0387	Y	SYN
4.1	Düll, B.	1999	Report on validation of analytical method – AW-207/1 Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland 72794, 01.04.1999 Syngenta File N° MK360/0495	Y	SYN

Annex point / reference number Doc IIIA	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner (1)
4.1	Düll, B.	1999a	Validation of analytical method AK-207/2 Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland 78027, 12.10.1999 Syngenta File N° MK360/0550	Y	SYN
4.1	Düll, B.	1999b	Thiabendazol – By-products and supplementary tests Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland AK-207/2, 13.10.1999 Syngenta File N° MK360/0549	Y	SYN
4.1	Düll, B.	2000	MK 360 – Thiabendazole – Statement on the analytical method AK-207/2 Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland 05.07.2000 Syngenta File N° MK360/0565	Y	SYN
4.1	Peterson, R	1998	Validation study (Part A) for Method M-021- HPLC method for the determination of Thiabendazole in simulated tank mixes, technical Thiabendazole and formulated Thiabendazole Merck Research Laboratories, Hillsborough Road, Three Bridges, New Jersey 08887-0450, USA Syngenta File N° MK360/0133		
4.1		1993	HPLC method for the determination of the Chlorinated Impurities in Thiabendazole Merck Manufacturing Division, MMD Standards and Administration, Merck & Co., Inc., Rahway, New Jersey 07065, USA Syngenta File N° MK360/0132		
4.2	Fisier, J	1994	Terrestrial Field Dissipation for thiabendazole in wheat Analytical Bio-Chemistry Laboratories, Inc., Field and Analytical Chemistry Programs, 7200 E. ABC Lane, Columbia, MO 65202-8015, USA Syngenta File N° MK360/0081		
4.2	Gentile, B.		Statement on method for the analysis of thiabendazole (MK 360) and 5-OH-thiabendazole (NOA 415696 in animal tissues Syngenta Crop Protection AG, Basel, Switzerland Syngenta File N° MK360/0579	Y	SYN
4.2	Watt, M.T. et, al.	1982	Determination of Thiabendazole and 5-hydroxythiabendazole in human serum by fluorescence-detected high-performance liquid chromatography J. of Chromatography, 230, 1982, pp. 79-86 Syngenta File N° MK360/0173	Y	SYN
4.2	Justin J.	1988	Fluorescence Method for the Determination of Thiabendazole in Water Merck Research Laboratories, Rahway NJ, United States METH. NO. M-042, 13.06.1989 - > 27.04.1988 Syngenta File N° MK360/0082	Y	SYN
4.2	Justin, J.	1990	Residue Assay Method and Residue Study for	Y	SYN

Annex point / reference number Doc IIIA	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner (1)
			Thiabendazole in Chicken Tissue and Eggs Merck & Co. Inc., Rahway NJ, United States MRID 40789818, MRID 00123329, 18.05.1990 Syngenta File N° MK360/0048		
4.2	Khan, M.A.	1992	Air Sampling and Analysis – Cassette Rinse Method Merck Research Laboratories, Three Bridges, United States LC-083, 15.07.1992 Syngenta File N° MK360/0151		SYN
4.2	Arenas, R.V.	1994	HPLC Fluorescence Method for the Quantitation of Thiabendazole residues and the metabolites 5-hydroxythiabendazole and the ulphate conjugate of 5-hydroxythiabendazole in milk Merck Research Laboratories, Three Bridges, United States M-028.1 REVISION 1, 25.04.1994 Syngenta File N° MK360/0223	Y	SYN
4.2	Arenas, R.V.	1994a	HPLC Fluorescence Method for the quantitation of thiabendazole residues and the metabolites 5-hydroxythiabendazole and benzimidazole in animal tissue Merck Research Laboratories, Three Bridges, United States M-027 (NEW), 19.05.1994 Syngenta File N° MK360/0224	Y	SYN
4.2	Arenas, R.V.	1994c	HPLC Fluorescence Method for the quantitation of thiabendazole residues and the metabolites 5-hydroxythiabendazole and benzimidazole in chicken egg Merck Research Laboratories, Three Bridges, United States M-025.1 (NEW), 19.05.1994 Syngenta File N° MK360/0225	Y	SYN
4.2	Arenas, R. Kruplak J.F.	1994	Residue Analytical Enforcement Method for Thiabendazole, 5-Hydroxythiabendazole and the Sulfate Conjugate of 5-Hydroxythiabendazole in Bovine Milk + Independent laboratory confirmation Merck Research Laboratories, Three Bridges, United States 26.05.1994 Syngenta File N° MK360/0051	Y	SYN
4.2	Arenas, R.V. Kruplak, J.F.	1994	Residue Analytical Enforcement Method for Thiabendazole, 5-Hydroxythiabendazole and benzimidazole in Chicken Egg + Independent laboratory confirmation Merck Research Laboratories, Three Bridges, United States 26.05.1994 Syngenta File N° MK360/0050	Y	SYN
4.2	Arenas, R.V. Mulkey N.S.	1994	Residue Analytical Enforcement Method for Thiabendazole, 5-Hydroxythiabendazole and Benzimidazole in Animal Tissue + Independent Laboratory Confirmation	Y	SYN

Annex point / reference number Doc IIIA	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner (1)
			Merck Research Laboratories, Three Bridges, United States 26.05.1994 Syngenta File N° MK360/0052		
6.1.1/01	Lankas, G.R:	1981	Thiabendazole veterinary (Lot ERM-211) - Acute oral toxicity study in rats. Merck Laboratories, West Point, United States 81-2691, 06.04.1981 Syngenta File N° MK360/0035	Y	SYN
6.1.2/01	Blaszcak, D.L. and Lankas, G.R.	1987	Thiabendazole: Acute dermal toxicity study in rabbits. Bio/Dynamics Inc., East Millstone NJ, United States 86-5505, 21.01.1987 Syngenta File N° MK360/0003	Y	SYN
6.1.3/01	Gurman, J.L.	1981	Acute inhalation toxicity study in rats. Hazleton Laboratories America Inc., Vienna, United States 81-9003, 23.10.1981 Syngenta File N° MK360/0004	Y	SYN
6.1.4/01	Orr, H.L.	1961	Skin study in rabbits. Merck Research Laboratories, West Point, United States 61-3017, 27.06.1961 Syngenta File Nº	Y	SYN
6.1.4/02	Lankas, G.R.	1981	Thiabendazole veterinary (Lot ERM-211) - Primary dermal irritation study in rabbits Merck Sharp & Dohme Research Laboratories, West Point, United States 81-2692, 06.04.1981 Syngenta File Nº	Y	SYN
6.1.4/03	Orr, H.L.	1961	Eye irritation study in rabbits. Merck Research Laboratories, West Point, United States 61-3018, 27.06.1961 Syngenta File Nº	Y	SYN
6.1.4/04	Lankas, G.R.	1981	Thiabendazole veterinary (Lot ERM-211) - Primary eye irritation study in rabbits Merck Sharp & Dohme Research Laboratories, West Point, United States 81-2693, 06.04.1981 Syngenta File Nº	Y	SYN
6.1.5/01	Peck, H.	1966	Thiabendazole - Cutaneous sensitization in the Guinea pig. Merck Institute for Therapeutic Research, Merck Sharp & Dohme Research Laboratories, Merck & Co., Inc., West Point, Pa, USA 66-0185, 31.03.1966 Syngenta File N° MK360/0036	Y	SYN
6.1.5/02	Cantoreggi, S.	1998	Skin sensitization in the Guinea Pig (Maximization Test) Novartis crop Protection AG 973077, 12.01.1998	Y	SYN
6.2/01	Tocco, D.J. et, al.	1965	Absorption, metabolism and excretion of thiabendazole in man and laboratory animals.	Y	SYN

Annex point / reference number Doc IIIA	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner (1)
			Merck Institute for Therapeutic Research and Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey, USA Toxicology and Applied Pharmacology, 9, 31-39 (1966) Syngenta File N° MK360/0002		
6.2/02	Craine, E.M.	1990	A metabolism study in rats with ^{14}C-thiabendazole. WIL Research Laboratories Inc., Ashland, Ohio, United States WIL-146002, 29.8.1990 Syngenta File N° MK360/0001	Y	SYN
6.3.1/01	Bagdon, W.J.	1977	Thiabendazole: Six-week pilot study in mice. Merck Research Laboratories, West Point, USA 77-004-0, 24.08.1977 Syngenta File Nº	Y	SYN
6.3.1/02	Usui, T.	1989	5-Week oral toxicity study in rats of Thiabendazole. Banyu Pharm., Development Research Lab., Osato-gun, Japan 86-9819 and 87-9809, 15.06.1989 Syngenta File N° MK360/0007	Y	SYN
6.4.1/01	Kangas, L. and Lankas, G.R.	1989	Thiabendazole - A 14-week oral toxicity study in the Albino rat. Bio-Research Laboratories Ltd., Senneville Quebec, Canada 89-9014, 04.12.1989 Syngenta File N° MK360/0008	Y	SYN
6.4.1/02	Batham, P. and Lankas, G.R.	1990	Thiabendazole - A 14-week oral toxicity study in the Beagle dog. Bio-Research Laboratories Ltd.., Senneville Quebec, Canada 89-9010, 17.01.1990 Syngenta File N° MK360/0009	Y	SYN
6.4.1/03	Myers, B. A. and Lankas, G.R.	1990	Thiabendazole - A 14-week dietary toxicity study in rats. Hazleton Laboratories America Inc., Rockville, United States 90-9002, 13.12.1990 Syngenta File N° MK360/0010	Y	SYN
6.5/01	Lankas, G.R.	1993	Thiabendazole - Fifty-three-week oral toxicity study in dogs. Merck Laboratories, West Point, United States 91-068-0, 20.01.1993 Syngenta File N° MK360/0011	Y	SYN
6.3.2/01	Cavagnaro, J. and Lankas, G.R.	1989	Thiabendazole - 23-Day dermal toxicity study in rabbits. Hazleton Laboratories America Inc., Vienna, United States 89-9011, 20.09.1989 Syngenta File N° MK360/0012	Y	SYN
6.6.1/01	Shirasu, Y. Moriya, M. and Kato, K.	1976	Mutagenicity testing on Thiabendazole (TBZ) in microbial systems, Host-mediated assay The Institute of Environmental Toxicology, Tokyo, Japan	Y	SYN

Annex point / reference number Doc IIIA	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner (1)
			76-9814, 01.09.1976 Syngenta File N° MK360/0013		
6.6.6/01	Shirasu, Y. Teramoto, S. and Kaneda, M.	1976	Dominant lethal studies with Thiabendazole in mice. The Institute of Environmental Toxicology, Tokyo, Japan 76-9817, 01.09.1976 Syngenta File N° MK360/0016	Y	SYN
6.6.3/01	Lankas, G.R. and Storer, R.D.	1989	Thiabendazole in vitro DNA alkaline elution/rat hepatocyte assay Merck Research Laboratories, West Point, PA, USA 89-8312, 12.05.1989 Syngenta File Nº MK360/0021	Y	SYN
6.6.2/01	Shirasu, Y. Tezuka, H. Hemmi, R. Murakami, N.	1976	Cytogenetic studies with Thiabendazole in cultured human fibroblasts. The Institute of Environmental Toxicology, Tokyo, Japan NONE, 01.09.1976 Syngenta File N° MK360/0014	Y	SYN
6.6.4/01	Gallaway, S. M. and Lankas, G.R.	1994	Thiabendazole - Assay for chromosomal aberration in mouse bone marrow. Merck Research Laboratories, West Point, PA, USA 94-8603, 11.07.1994 Syngenta File N° MK360/0022	Y	SYN
6.6.4/02	Shirasu, Y. Tezuka, H. Hemmi, R. Murakami, N.	1976	Cytogenetic studies with Thiabendazole in rat bone marrow cells. The Institute of Environmental Toxicology, Tokyo, Japan NONE, 01.09.1976 Syngenta File N° MK360/0015	Y	SYN
6.6.3/02	Lankas, G.R. and Sina, J.F.	1993	Thiabendazole - Microbial mutagenesis assay in (*Salmonella typhimurium* and *Escherichia coli*) Merck Research Laboratories, West Point, PA, USA 92-8074 and 92-8079, 28.04.1993 Syngenta File N° MK360/0023	Y	SYN
6.7/01	Bagdon, W.J.	1979	Thiabendazole - Lifetime carcinogenic study in mice. Merck Research Laboratories, West Point, PA, USA 77-014-0, 12.12.1979 Syngenta File N° MK360/0024	Y	SYN
6.7/02	Lankas, G.R. and Wolfe, G.W.	1993	Thiabendazole - 106-Week dietary toxicity /carcinogenicity study in rats. Hazleton Washington, Inc., Vienna, USA and Merck Research Laboratories, West Point, PA, USA 90-9009, 27.09.1993 Syngenta File N° MK360/0025	Y	SYN
6.8.1/01	Hoberman, A.M.	1989	Thiabendazole - Oral developmental toxicity study in rabbits. Argus Research Lab. Inc., Horsham, USA 89-9005, 27.10.1989 Food and Chemical Toxicology, 31, 199-207, (1993) Syngenta File N° MK360/0029	Y	SYN
6.8.1/02	Wise, L.D.	1990	Thiabendazole - Oral development toxicity study in rats Merck Research Laboratories, West Point, PA, USA	Y	SYN

Annex point / reference number Doc IIIA	Author(s)	Year	Title, Source, Company, Report No GLP or GEP status (where relevant), Published or not	Data Protection Claimed Y/N	Owner (1)
			90-713-0, 28.11.1990 Food and Chemical Toxicology, 31, 199-207 (1993) Syngenta File N° MK360/0030		
6.8.1/03	Lankas, G.R. and Wise, D.L.	1991	Thiabendazole - Oral development toxicity study in rabbits. Merck Research Laboratories, West Point, PA, USA 90-734-0, 10.06.1991 Food and Chemical Toxicology, 31, 199-207, (1991) Syngenta File N° MK360/0031	Y	SYN
6.8.2/01	Wise, D.L. Lankas, G.R.	1992	Thiabendazole - Two-generation dietary reproduction study in rats. Merck Research Laboratories, West Point, PA, USA 90-733-0, 21.05.1992 Food and Chemical Toxicology, 32, 239-246, (1994) Syngenta File N° MK360/0027	Y	SYN
6.10	Lankas, G.R.	1995	Thiabendazole - Fourteen-week dietary thyroxine clearance study in rats with a 14-week recovery period. Merck Laboratories, Westpoint, United States 94-024-0, 16.02.1995 Syngenta File N° MK360/0026	Y	SYN

Annex IIIA	Author(s) Year Title MSD Report No. Source (if different)	GLP/ GEP Y/N	Publish. or not Y/N	Owner	Data prot.
7.1.1.1/01	Dykes, J. and Kabler, K. 1990 Photochemical Degradation:Determination of the Photolysis Rate of [14C]-Thiabendazole on the Surface of the Soil. MSD Report No.: 37638 Source: Analytical Bio-Chemistry Laboratories, Columbia, USA	Y	N	MSD	Y
7.2.1/03	Daly, D. 1990 Anaerobic Soil Metabolism of [14C]-Thiabendazole. MSD Report No.: 37640 Source: Analytical Bio-Chemistry Laboratories, Columbia, USA	Y	N	MSD	Y
7.2.1/01	Daly, D. 1991 Aerobic Soil Metabolism of [^{14}C]-Thiabendazole. MSD Report No.: 37639 Source: Analytical Bio-Chemistry Laboratories, Columbia, USA	Y	N	MSD	Y

7.1.2/01	Dykes, J. 1989 Soil Adsorption/Desorption with Thiabendazole. MSD Report No.: 37635 Source: Analytical Bio-Chemistry Laboratories, Columbia, USA	Y	N	MSD	Y
7.1.3/01	Aharonson, N. and Kafkafi, U. 1975 Adsorption, Mobility and Persistence of Thiabendazole and Methyl-2-benzimidazole-carbamate in Soils. J. Agr. Food Chem. 23, 720, 1975b.	N	Y	N	N
7.1.3/02	WARF 1976 Soil Leaching Study: Column Method Radiolabeled Thiabendazole. Source: WARF Institute, Inc., Madison, Wisconsin, USA WARF Report No.: report c	N	N	MSD	N
7.1.4/01	Schroeder, C. and Steele, J. 1978 Soil Mobility of Thiabendazole Aerobically Aged in Soil and Photodegraded Thiabendazole. MSD Report No.: none Source: WARF Institute, Inc., 3301 Kinsman Blvd, Madison, Wisconsin, USA	N	N	MSD	N
7.1.1.1.1/01	Kabler, K. and Dykes, J. 1989 Stability in Water: Hydrolysis as a Function of pH at 25°C of [14C]-Thiabendazole. MSD Report No.: 37636 Source: Analytical Bio-Chemistry Laboratories, Columbia, USA	Y	N	MSD	Y
7.1.1.1.2/01	Flynn, J. 1994 Determination of the Aqueous Photolysis Rate [14C]-Thiabendazole. MSD Report No.: 41285 Source: Analytical Bio-Chemistry Laboratories, Columbia, USA	Y	N	MSD	Y
7.1.1.2.1/01 (according to TNsG: 7.1.2.2.2 / 01)	Vonk, J.W. 1988 Biodegradation of Thiabendazole in an Aerobic Water/Sediment System. Source: TNO Division of Technology for Society, Delft, The Netherlands TNO Report No.: R88/166	N	N	MSD	Y
7.1.1.1.2/02	Van der Kolk, J. 1998a MK 360 (Thiabendazole) ready biodegradability CO_2 evolution test (modified Sturm test). Springborn Labs. CH - 9326 Horn, Switzerland				

7.1.2. /02 (according to TNsG: 7.1.2.2.2 / 02)	Ulbrich, R. 1999 MK 360 (CGA 28020): Degradation and of ^{14}C-Phenyl-Labelled MK 360 in Two Aerobic. Source: Aquatic Systems under Laboratory Conditions, Novartis Crop Protection AG, Environmental Safety, Ecochemistry CH – 4002 Basel, Switzerland	Y	N		
7.2.1 / 02	Phaff, R. 1999 Rate of Degradation of ^{14}C-Phenyl-Labelled MK 360 in one Soil under Various Laboratory Conditions at 20°C and 30°C. Study No.: 98RP06 Source: Novartis Crop Protection AG Basel, Switzerland	Y	N	-	N
7.1.1.1.2/02	Schmidt, E. 2002 Quantum Yield of the Direct Photochemical Degradation of Thiabendazole in Aqueous Solution. Physical Chemistry 4002 Basel, Switzerland Proj.No L01-008389				
7.3.1 / 01	Stamm, E 1997 Atmospheric Oxidation of Thiabendazole MK-360 by Hydroxyl Radicals; Rate Estimation Report No.: 95A97067SM Source: Novartis Crop Protection AG Environmental Safety Chemodynamics CP 2.44 CH-4002 Basel				
7.2.2.2./01	Jacobson, B 1994a MERTECT 340-F (TECTO Flowable) Terrestrial Field Dissipation for Thiabendazole in Soybeans. MSD Report No.: 92516 Source: Analytical Bio-Chemistry Laboratories, Columbia, USA	Y	N	MSD	Y

7.2.2.2/02	Jacobson, B 1994b MERTECT 340-F (TECTO Flowable) Terrestrial Field Dissipation for Thiabendazole in Soybeans. MSD Report No.: 92678 Source: Analytical Bio-Chemistry Laboratories, Columbia, USA	Y	N	MSD	Y
7.2.2.2/03	Jacobson, B 1994c MERTECT 340-F (TECTO Flowable) Terrestrial Field Dissipation for Thiabendazole in Wheat. MSD Report No.: 92530 Source: Analytical Bio-Chemistry Laboratories, Columbia, USA	Y	N	MSD	Y
7.5.3.1.1./02	Grimes, J. and Jaber, M. 1989a Technical Thiabendazole: An Acute Oral Toxicity Study with the Bobwhite. Wildlife International Report No.: 105-138 Source: Wildlife International, Easton, Maryland, USA	Y	N	MSD	N
7.5.3.1.2./02	Grimes, J. and Jaber, M. 1989b Technical Thiabendazole: A Dietary LC50 Study with the Bobwhite. Wildlife International Report No.: 105-136 Source: Wildlife International, Easton, Maryland, USA	Y	N	MSD	N
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7.4.1.1./01	Beglinger, J.M. and O'Boyle, R.J. 1989a Acute Aquatic Effects of Thiabendazole on the Bluegill Sunfish, *Lepomis macrochirus*. Eastman Kodak Report No.: EN-413-GWN001-2 Source: Health and Environment Labs, Eastman Kodak Company, New York, USA	Y	N	MSD	N
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7.4.1.1./04	Holmes, C.M., Swigert, J.P. and Smith, G.J. 1992 Thiabendazole: A 96-Hour Static Acute Toxicity Test with the Bluegill Sunfish, *Lepomis macrochirus*. Wildlife International Report No.: 105-118A Source: Wildlife International, Easton, Maryland, USA	Y	N	MSD	Y
7.4.1.2./01	Surprenant, D.C. 1989a Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow-Through Conditions. MSD Report No.: 89-5-2986 Source: Springborn Life Sciences, Inc., Wareham, MA, USA	Y	N	MSD	Y

7.4.1.1./03	Surprenant, D.C. 1989b Acute Toxicity of Thiabendazole to Sheepshead Minnow (*Cayprinodon variegatus*) Under Flow-Through Conditions. MSD Report No.: 89-3-2957 Source: Springborn Life Sciences, Inc., Wareham, MA, USA	N	N	MSD	Y
7.4.3.2./01	Holmes, C.M. and Swigert, J.P. 1992 Thiabendazole: An Early Life-Stage Toxicity Test with the Fathead Minnow (*Pimephales promelas).* Source: Wildlife International, Easton, Maryland, USA Wildlife International Report No.: 105A-111	Y	N	MSD	Y
7.4.3.1./02	Wilson, B.F., LeBlanc, G.A. and Maston, J.D. 1982 The Toxicity of MERTECT Fungicide to Rainbow Trout (*Salmo gairdneri)* Embryos and Larvae. EG&G Report No.: BW-82-1-1099 Source: EG&G, Bionomics, Aquatic Toxicology Laboratory, Wareham, Mass., USA	N	N	MSD	N
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7.4.3.4./01	LeBlanc, G.A., Mastone, J.D. and Surprenant, D.C. 1981 The Chronic Toxicity of MERTECT Fungicide to the Water Flea (*Daphnia magna*). EG&G Report No.: BW-81-6-900 Source: EG & G, Bionomics, Aquatic Toxicity Laboratories, Wareham, Mass., USA	N	N	MSD	N
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7.5.2.2.	Meister, A. 2002 Effects of MK360B on reproduction of the collembola *Folsomia candida* in artificial soil IBACON GmbH. Report No. 11382016	Y	N	MSD	N
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7.5.4.1./02	Hargreaves, N.J. and Kennedy, P.J. 2003 Acute Contact and Oral Toxicity of Technical Material to the Honeybee (*Apis mellifera*). Report No. RJ3396B Syngenta file No.: 2021847 Syngenta Jealott´s Hill International Reasearch Centre Bracknell, Berkshire RG42 6EY, UK	Y	N		N
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