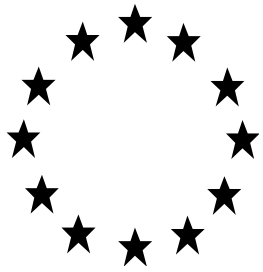
Directive 98/8/EC concerning the placing biocidal products on the market

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

Assessment Report



Coumatetralyl

Product-type PT 14 (Rodenticides)

20 February 2009

RMS - DK

COUMATETRALYL (PT14)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 20 February 2009 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 Coumatetralyl as product-type 14 (Rodenticides), 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.

Coumatetralyl (CAS no. 5836-29-3) was notified as an existing active substance, by Bayer Environmental Science, Lyon, France, hereafter referred to as the applicant, in product type 14.

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, Denmark 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 Coumatetralyl as an active substance in Product Type 14 was 28 March 2004, in accordance with Annex V of Regulation (EC) No 2032/2003.

On 18 March 2004, the applicant Bayer Environmental Science, Lyon, France subitted a dossier on coumatetralyl to the Danish competent authorities. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 28 September 2004.

On 29 September 2005, 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 7 October 2005. The competent authority report included a recommendation for the inclusion of Coumatetralyl in Annex I to the Directive for PT14.

In accordance with Article 12 of Regulation (EC) No 2032/2003, the Commission made the competent authority report publicly available by electronic means on 13 February 2006. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

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

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

2 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

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

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 20 February 2009.

1.2. Purpose of the assessment report

This assessment report has been developed and finalised in support of the decision to include Coumatetralyl in Annex I to Directive 98/8/EC for product type 14. The aim of the assessment report is to facilitate the authorisation in Member States of individual biocidal products in product type 14 that contain Coumatetralyl. 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 information and conclusions of this assessment report are based on data protected under the provisions of Directive 98/8/EC, This report shall not be used to support any authorisation/registration outside the context of that Directive, e.g. in other countries, unless the applicant has demonstrated legitimate access to the information on which this report is based.

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 coumatetralyl for the product type 14, which will fulfil the requirements laid down in Article 5 of Directive 98/8/EC. This conclusion is however subject to:

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

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

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

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

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

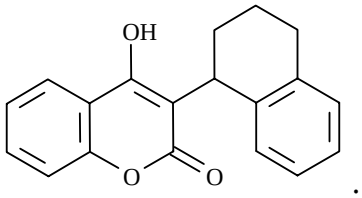
2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

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

Identity

Coumatetralyl, IUPAC name: 4-hydroxy-3-(1, 2, 3, 4-tetrahydro-1-naphthyl) coumarin, CAS number [5836-29-3], is a rodenticide produced by Bayer Environmental Science at Bayer AG site in Uerdingen (Germany). Coumatetralyl technical grade produced by Bayer AG is a racemic mixture of R and S enantiomers is also called Racumin S technical (ENE 1183b). The molecular formular of the active substance is $C_{19}H_{16}O_3$ and the structural formula:



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Analysis of five technical grade batches which are representative of the current manufacturing process demonstrated a mean purity of 99.3% w/w in compliance with Bayer environmental science specification. Coumatetralyl technical does not contain additives and all impurities above the level of 1 g/kg have been fully identified and the corresponding methods of analysis have been developed.

Physical and chemical properties

Coumatetralyl technical is a white to yellow-grey crystalline powder with a characteristic slight odour and a melting point of 168.8°C. Its molecular mass is 292.3 g/mol and its relative density is 1.328 at 20°C.

The vapour pressure is found to be less than 1.0E-05 hPa at 20°C. The water solubility of coumatetralyl technical is 4.40E-03 g/l (pH 5.1) at 20°C and the dissociation constant in water/acetone is 5.3.

Coumatetralyl technical is very soluble in dimethylsulfoxide (>250 g/l) and less soluble in xylene (2.7 g/l). Its octanol/water partition coefficient is 2.9 in demineralised water (pH 5.8) at 23°C. The technical grade is not surface active.

The exothermal decomposition of the technical grade starts at 195°C. It is not highly flammable and does not liberate gases in hazardous amount upon contact with water or undergo spontaneous combustion. Coumatetralyl technical has no explosive or oxidising properties.

The recommended container materials for coumatetralyl technical are plastic materials e.g. PE or high-grade steel. Aluminium, unprotected steel or iron is not suitable for container material.

Coumatetralyl has no critical physico-chemical properties; therefore, the active substance does not require any classification under the provisions of directive 67/548/EEC.

Methods of analysis

The identification and quantification of coumatetralyl as manufactured is performed using the CIPAC method 189. Nevertheless for quality control purpose a HPLC method with UV detection is preferred. Methods of analysis for all impurities are also described in the confidential sections. The method of analysis for one of the impurities in not acceptable due to missing validation data, and should be provided at product authorisation level.

The identification and quantification of coumatetralyl in formulation is performed using a HPLC method with UV detection.

HPLC-MS/MS methods were developed to analyse residues in soil and water with the respective limits of determination of 1 µg/ kg of soil and 0.05 µg/l of water. Residues in air were analysed with a HPLC-UV-DAD method with a limit of quantification of 0.030 mg/m^3 of air. The analysis for residue in animal tissues is performed using a HPLC method with fluorescence detection and its limit of detection is 0.1 mg/kg.

An analytical method for the determination of residues of coumatetralyl in/on food or feedingstuffs is required at product authorisation in case of accidental or deliberate contamination, as agreed at TMII04.

2.1.2. Intended Uses, Efficacy and Humaneness

Intended Use

Coumatetralyl is used to control rodents, especially rats. The uses are listed in Appendix II.

Efficacy

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.

A total of 4 trials were performed in laboratories on rats (*Rattus norvegicus*) to evaluate the acceptance, the palatability and the efficacy of the coumatetralyl containing product Racumin® Paste. A lethal dose of coumatetralyl in Racumin® Paste can be taken within the first day of a treatment but complete mortality among rats needs more than one day of access to the product. The palatability is unaffected by up to 12 month storage period at 25°C or up to 8 weeks at 50°C.

A total of 7 field trials were performed on rats (*Rattus rattus* and *Rattus norvegicus*) to evaluate the palatability and the efficacy in different farms, warehouse, composting plant, sewerage system and drain in Germany and in a building plant in Malaysia. Six of these tests showed an excellent efficacy even under tropical conditions. One field trial under extremely humid conditions showed that Racumin® Paste remained attractive to rats as long as it was not covered with mold.

Based on these results, coumatetralyl in Racumin Paste is evaluated to be efficient as a rodenticides against *Rattus rattus* and *Rattus norvegicus*.

Anticoagulant resistance is a major loss of efficacy in practical conditions where the anticoagulant has been applied correctly, the loss of efficacy being due to the presence of a strain of rodent with a heritable and commensurately reduced sensitivity to the anticoagulant. The Rodenticide Resistance Action Committee of Crop Life International (RRAC) published a Technical Monograph (RRAC 2003a) in which anticoagulant resistance management strategies are proposed on the best knowledge of rodent control. This strategy is described in document IIB.

Humaneness

The use of coumatetralyl as an anticoagulant rodenticide that could cause suffering of vertebrate target organisms as concluded in "Assessment of Humaneness of Vertebrate Control Agents" (Pesticides Safety Directorate, UK, 1997): " It is concluded that all of the anticoagulant rodenticides have the capacity to cause haemorrhage at multiple sites. Although there is some evidence to indicate that the frequency and actual location of these sites may vary with both the particular compound and the sex of the animal involved the accumulation of blood in a restricted site, leading to severe discomfort, cannot be ruled out for any anticoagulant. As severe discomfort, which can last for several days, occurs in a large proportion of all the reported studies anticoagulant rodenticides must be regarded as being markedly inhumane."

However, the use of anti-coagulant rodenticides is necessary as there are at present no other valuable measures available to control the rodent population in the European Union. Rodent control is needed to prevent disease transmission, contamination of food and feeding stuffs and structural damage. It is recognised that such substances do cause pain in rodents but it is considered that this is not in conflict with the requirements of Art. 5.1 of the BPD `to avoid unnecessary pain and suffering of vertebrates`, as long as effective, but comparable less painful alternative biocidal substances or biocidal products or even non-biocidal alternatives are not available. Such a comparative assessment is not under the scope of this report, but should be preformed when possible alternatives have been evaluated and all data are available.

2.1.3. Classification and Labelling

Proposed classification/labelling for the active substance, coumatetralyl, following evaluation:

Classification/Labelling	as in Directive 67/548/EEC	
Class of danger	T+	Very toxic
R phrases	R61:	May cause harm to the unborn child.
	R 26/28:	Very toxic by inhalation and if swallowed.
	R 24:	Toxic in contact with skin
	R 48/23/24/25:	Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.
	R 52/53:	Harmful to aquatic organisms may cause long-term adverse effects in the aquatic environment.
S phrases	S 45:	In case of accident or if you feel unwell, seek medical advice immediately (show label where possible).
	S53:	Avoid exposure – obtain special instructions before use.
	S61:	Avoid release to the environment. Refer to special instructions in safety data sheets.

However, the classification for reproductive toxicity, R61 is still under debate and will be taken up by the Risk Assessement Committee under EChA.

Proposed classification for the representative biocidal product, Racumin® Paste, following evaluation:

Classification/Labelling	**as in Directive 99/45/EC**
Class of danger	Xn Harmful
R phrases	R 22: Harmful if swallowed R 43: May cause sensitisation by skin contact. 48/21/22: Harmful: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed
S phrases	S 2: Keep out of the reach of children S24 Avoid contact with skin S 35: This material and its container must be disposed of in a safe way. S 46: If swallowed, seek medical advice immediately and show this container or label.

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Human health effect assessment

- **Toxicokinetics**

Oral application of coumatetralyl is followed by rapid and efficient (75%(m) and 86%(f)) absorption in the rat. The substance is excreted slowly and dependent on sex and the number of applications. The primary route of excretion is via the urine and to a smaller extend via faeces. The half-lives of the terminal phase after a single dose application were about 71 and 46 hours for male and female rats, respectively. After multiple dosing of males, half-life of the terminal phase was 36 hours. Coumatetralyl reaches a relative high concentration in liver and skin.

Coumatetralyl is extensively metabolised via hydroxylation of the tetrahydronaphtyl moiety. Four metabolites were identified: the main metabolite 13-hydroxy-coumatetralyl (MT 0315A) and three isomers of the main metabolite (MT 0315C, MT 0315D, MT 0315F). In urine two further metabolites (MT 0315B and MT 0315E) could be verified.

- **Health hazard of the active substance**

Coumatetralyl is highly toxic by acute oral exposure. The oral LD_{50} value of coumatetralyl in the most sensitive species (rat) tested is 30/15 mg/kg bw for males and females, respectively. Other mammalian species (mouse, dog cat, guinea pig, and rabbit) are less susceptible to single oral doses of coumatetralyl.

No acute and short-term inhalation guideline-studies are available; the justification to waive these studies for coumatetralyl a.i. is based on coumatetralyl physical-chemistry data showing that it is not volatile and that significant levels in the air are unlikely and the most relevant modes of exposure for operators and consumers are by dermal contact or oral absorption. Two inhalation studies performed in rats and mice in 1982 indicate high inhalation toxicity although they are not considered as reliable because of major methodological and reporting deficiencies with the current guideline. However the studies can be used as supportive for the proposal for classification/labelling of coumatetralyl. Based on such inherent properties of the substance the possibility of inhalation of the technical compound to the operator in the manufacturing process must also be taken into account.

Following dermal administration of coumatetralyl to rats, lower toxicity than by the oral route was observed. The LD_{50} value is between 100 and 500 mg/kg bw for males and 258 mg/kg bw for females. The lowest value is supported by three non-guideline studies.

Therefore, classification/labelling for acute toxicity should be:

T+; R24 - R26/28: Toxic in contact with skin, very toxic by inhalation and if swallowed.

The potential of coumatetralyl to cause skin and eye irritation was assessed in rabbits. Coumatetralyl caused no primary irritation on the skin or the eye. Classification/labelling for irritation/corrosivity is not necessary.

No skin-sensitising effects of coumatetralyl were observed in the Buehler Patch test on female guinea pigs. Therefore classification/labelling is not required.

A subchronic toxicity study of coumatetralyl has been conducted in rat by oral dosing. A daily intake of approx. 0.1 mg/kg bw caused a mortality of 70% in male and 25% in female rats. All effects seen in the subchronic study were directly or indirectly related to the well-known pharmacological effects of coumatetralyl on blood clotting. Effects observed were generally haemorrhages and pallor and reduced activity before dead of the animal. Blood clotting time was consistently (and statistically significantly) increased in both sexes at 85 ppm and above. A slight (5-10%) but statistically significant increase in blood clotting time was observed in males fed 40 ppm at all time points except the last one. In females of the 40 ppm group, only one time point showed statistically significant prolonged clotting time. The effect on blood clotting time was dose dependent in both sexes.

As no measurements of the prothrombin levels (possibly more sensitive parameter) were performed, and as no other study is available on subchronic or chronic toxicity of coumatetralyl, the RMS has chosen a conservative interpretation of the result of this study. Therefore, the slight but significant effect on blood clotting time that was seen at all but one time point in males at 40 ppm (0.021 mg/kg bw/day) is regarded as adverse.

The NOAEL is therefore set at 13 ppm equivalent to 0.0068 mg coumatetralyl/kg bw/day in males and 0.0083 mg coumatetralyl/kg bw/day in females.

No further subchronic or chronic toxicity studies have been conducted, despite the fact a subchronic study in a second species and a long term toxicity/carcinogenicity study is required as part of the common core data requirements for toxicological documentation.

The justifications for not performing these studies were based on several considerations:

Justifications for a waiver for studies in a second animal species were based on the weight of evidence which indicates that the already well-characterised pharmacological properties of this compound would also be observed in the dog treated at very low doses in a sub-chronic study and that new adverse effects which might have an impact on risk assessment are unlikely to be discovered in this species. This is further supported by published data of two 7-day studies conducted in dogs with coumatetralyl.

Justification for a waiver for long-term/carcinogenicity studies is based on the lack of mutagenic/genotoxic effects, the absence of any other effects that may lead to non-genotoxic carcinogenesis, the absence of any carcinogenic effects following long-term administration of warfarin, a coumarin compound, in humans and the absence of potential for long-term exposure of the public population.

The waiving of the subchronic and chronic studies, as well as the carcinogenicity studies are accepted with the provision that reference to exposure conditions will be referred to in the Annex I listing of coumatetralyl.

Based on the long half-life of coumatetralyl in the liver of rats observed in the metabolic studies resulting in increased mortality seen in the subchronic study the following classification/labelling for repeated dose toxicity according to Directive 67/548/EEC is proposed:

T;R48/23/24/25: Toxic, danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.

No evidence for genotoxic potential was observed in the various in-vivo or in-vitro tests. Thus, coumatetralyl is unlikely to pose a genotoxic hazard to man and therefore a classification/labelling according to Directive 67/548/EEC is not necessary.

A multigeneration study, as required in the common core data requirements in the BPD directive is not available. The justification for waiving the study based on the consideration that high body levels following the premating period would render the animals susceptible to death by haemorrhage from the natural events of reproduction and parturition, and on the absence of potential long-term exposure of the public population was accepted by the RMS.

Teratogenicity studies were conducted in rat and rabbit, respectively. No effects on the developing foetus were seen either animal species tested.

In the rat study, the NOAEL were 0.14 mg/kg bw/day for embryotoxicity and 0.035 mg/kg bw/day for maternal toxicity. The NOAELs in the rabbit study were 0.025 mg/kg bw/day for embryotoxicity and 0.0125 mg/kg bw/day for maternal toxicity.

The negative results of the developmental studies with coumatetralyl in rat and rabbit do not indicate developmental toxicity of coumatetralyl. However, due to the vulnerability of the animals to the anticoagulant effect of coumatetralyl (and other anticoagulant rodenticides), standard guideline tests are expected to be less suited to reveal developemental effects of this class of substances. Coumatetralyl is structurally and mechanistically analogue to the human developmental toxicant warfarin. Classification of anticoagulant rodenticides for developmental effect was discussed by the Specialised Experts in October 2006. The experts unanimously agreed that the AVK rodenticides should collectively be regarded as human teratogens.

Therefore the other AVK rodenticides should be classified as Repr. Cat. 1; R61. At TM III 06 it was agreed that regardless the C&L decision on this issue, the CAR of AVKs under the BPD will be finalised taking into account the Specialised Experts conclusion. The RMS the thus proposes coumatetralyl to be classified Repr. cat.1; R61 "May cause harm to the unborn child".

- **Critical end-points**

Coumatetralyl is of very high acute toxicity by the oral route and the inhalation route and of high toxicity by the dermal route. The substance is not irritating to skin or eye and is not a skin sensitizer.

In the short term and repeated dose studies the blood clotting was the target effect of coumatetralyl, with significantly increased blood clotting time at low dosing levels (NOAEL 0.0068 mg/kg bw/day). Coumatetralyl is not considered to be genotoxic or carcinogenic or to affect the reproductive capability, although no long term studies were available due to the pharmacological well-known effect of this anticoagulant. The standard studies for developmental toxicities were negative. However, cross-reading to the structural analogue warfarin, a known human developmental toxicant resulted in the recommendation from the Specialised Experts to classify coumatetralyl as a developmental toxicant in category 1.

- **Reference values for the active substance**

$AEL_{subchronic}$ / AOEL (Acceptable-Operator-Exposure-Level)

The NOAEL for subchronic oral exposure of male rats is relevant for AEL calculation. A correction factor of 0.75 is applied to account for the observed oral absorption of 75% in male rats. The applicable assessment factors are 10 for intra-species differences and 10 for inter-species differences. In addition, an extra assessment factor of 3 is included in accordance with the decision of the TM for all anticoagulant rodenticides to take account of the severity of the effect on development. Thus, the following calculation leads to the $AEL_{subchronic}$:

$AEL_{subchronic} = 1.7 \times 10^{-2}$ µg/kg bw/day

AEL_{acute}

In accordance with the decision at TM II07, the acute AEL for coumatetralyl is based on the lowest NOAEL from a teratogenicity study, namely the rabbit development study. Default assessment factors of 10 for intra-species variability and 10 for inter-individual variability are applied. In addition, an extra assessment factor of 3 is included in accordance with the decision of the TM for all anticoagulant rodenticides to take account of the severity of the effect on development. A correction factor of 0.75 is applied to take account of the oral absorption. Thus, the following calculation leads to the AEL_{acute}:

$AEL_{acute} = 3.1 \cdot 10^{-2}$ µg/kg bw/day

- **Health effects of representative product**

The ability of coumatetralyl to penetrate the skin was examined: an in-vivo study in rats with Racumin® Paste demonstrated that after 8 hours of exposure the total amount of applied

radiolabelled material absorbed was 4.44%, 5.26%, 3.47%, and 4.47% of the applied dose at 8, 24, 72 and 168 hours post-application, respectively. An in-vitro study with rat and human skin shows that after 8 hours of exposure the total amount of radioactive material absorbed was 4.6 times greater for rat skin (1.441% of applied dose) than for human skin (0.316% of applied dose) during a period of 24 hours.

A dermal absorption value in humans of 1,14% is therefore used in the risk assessment based on extrapolation taking into consideration the worst case scenario including a dermal absorption of 5.26% in rat skin at 24 hours and a rat-to-human ratio of 4.6.

Racumin® Paste proved to be moderately toxic after oral application to rat. The LD_{50} cut-off value was 1000 mg/kg bw for female rats: Racumin®Paste was not toxic in contact with skin, the LD_{50} value was about 4000 mg/kg bw for male and female rats. It exhibits neither skin irritation nor eye irritation in the rabbit. In a Magnusson and Kligman study, the Racumin®Paste has shown a skin-sensitisation potential4.

Attribution of specific lower concentration limits for coumatetralyl containing products with respect of classification for repeated exposure was agreed in the technical committee for classification and labelling in May 2007.

Based on the overall information, the following classification/labelling for Racumin® Paste according to Directive 67/548/EEC (annex VI) and 99/45/EC is warranted: Xn; R22: Harmful if swallowed and Xn; R48/20/21/22 Harmful: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed and Xi; R43: may cause sensitisation by skin contact.

2.2.1.2. Human exposure assessment

Exposure and risk assessment for human health of coumatetralyl is based on the representative product Racumin®Paste. Exposure of humans to coumatetralyl can potentially take place during manufacture, use and disposal and by indirect exposure.

- *Primary exposure*

Due to the non-volatile nature of coumatetralyl and the pasty nature of the representative biocidal product it is reasonable to assume that inhalation and oral exposure are both negligible and need no further assessment. Therefore, the only relevant operator exposure scenario to be assessed is via the dermal route. Again, due to the paste formulation no exposure of the body by dust or spillage is foreseen. Therefore it can be concluded that dermal exposure to Racumin® Paste when handling the sachets during application and disposal is confined to exposure of the hands.

A product specific exposure study was conducted in Germany by Bayer CropScience AG based on the following worst case assumptions:

- The professional operator, wearing gloves or not when handling the bait sachets, spearing 100 g bait sachets onto wire for the placement in e.g. sewers, 20 bait sachets

4 A LLNA test was made available by the applicant after evaluation of the report.

per day (2 kg Racumin® Paste per day) during the application phase and removing 10 bait sachet per day assuming that 5 of them are partly eaten during the disposal phase.

- The amateur operator wearing no gloves, placing 100 g bait sachets into e.g. bait boxes, 5 bait sachets per day (0.5 kg Racumin® Paste per day) during the application phase and removing 3 bait sachets per day, assuming that 2 of them are partly eaten, during the disposal phase.

The results of this product specific study can be used as a basis for estimating the daily exposure of professionals and amateurs during application and disposal of Racumin® Paste. Decision of TM III-06 on the number of manipulations relevant in assessment of exposure for different types of rodenticide products was that the bait pastes, following the figures for wax blocks, would by handled by professionals around 75 times per day, 60 loadings and 15 disposals.

The dermal exposure estimates from the available study, adjusted to the agreed harmonised number of handlings, were converted to systemic exposure assuming 1.14% dermal absorption for coumatetralyl. The assessment was made for two scenarios: first taking into account exposure over a medium time period (corresponding to average exposure) and a second taking into account a worst case scenario. Results are summarised in table 2.2.

o *Secondary exposure*

Calculations of indirect exposure to coumatetralyl based on guidance exposure values from the TNsG indicate an exposure through transient mouthing by infants/children of 0.01g.

For the scenario of a child eating bait the TNsG indicates that a child could accidently ingest 5 g of bait.

2.2.1.3. Human health risk characterisation

o *Risk through primary exposure*

The exposure values derived above for average and worst case scenarios were compared with the systemic $AEL_{subchronic}$ of 0.017 µg/kg bw/day. For both scenarios the estimated systemic exposure of the professional and the amateur performing application and disposal phase accounts for not more than 87.6% of the proposed systemic AEL, each, even if no gloves are worn. The Margin Of Exposure (MOE) to the relevant $NOAEL_{subchronic,male}$ (6.8 µg/kg bw/day, corrected figure for oral absorption of 75%: 5.1 µg/kg bw/day) amounts to at least 342. The results are summarised in table 2.2.

Table 2.2: **Comparison of estimated systemic operator exposure to coumatetralyl during application and disposal in relation to the proposed $AEL_{subchronic}$ and corresponding MOE to the relevant NOAEL.**

User	Exposure figure	Gloves	Exposure [µg/kg bw/day]	% of AEL [0.0017 µg/kg bw/day]	MOE [5.1 µg/kg bw/day]*
Professional	Geometric mean	NO	0.011	**64.7%**	**$4.6 \cdot 10^2$**
		YES	0.000067	**0.39%**	**$7.6 \cdot 10^4$**
	Maximum	NO	0.0149	**87.6%**	**$3.4 \cdot 10^2$**
		YES	0.00044	**2.6%**	**$1.16 \cdot 10^4$**
Amateur	Geometric mean	NO	0.000086	**0. 5 %**	**$5.9 \cdot 10^4$**
	Maximum	YES	0.000277	**1.6%**	**$1.84 \cdot 10^4$**

Based on these results it can be concluded that for the intended use of Racumin® Paste no unacceptable risk is given for the professional and the amateur user even if no gloves are worn.

- *Risk through secondary exposure*

Comparison of the exposure through transient mouthing by infants/children and the acute AEL show an unacceptable health risk of 1226% of AEL_{acute} (0.031µg/kg bw/day) and the MOE 25.

The scenario of a child eating bait also shows an unacceptable risk, as the exposure accounts for 606451% of the AEL, with a MOE of only 0.05. Therefore, use of risk reduction measures as bittering agent addition to the product and use of tampered proof secured bait stations which are required with the Racumin® Paste product, as well as other risk reduction measures are necessary to reduce this risk of accidental poisoning as much as possible.

2.2.2 Environmental Risk Assessment

2.2.2.1. Environmental Effect assessment

Fate and distribution in the environment

Coumatetralyl is stable to hydrolysis and was degraded rapidly by light to a number of degradation products, of which salicylic acid was identified as a major product.

Coumatetralyl was not readily biodegradable under the conditions of the Closed Bottle Test and not inherently biodegradable under the conditions of the Zahn-Wallens/EMPA Test. However, the half-life in soil is less than 30 days (primary degradation not mineralization) under aerobic conditions but under anaerobic conditions, no degradation of coumatetralyl took place during 60 days.

Coumatetralyl can be classified as a moderately leachable compound in sand soil. In loamy sand and sandy loam no leaching of coumatetralyl was observed

Coumatetralyl is accumulated very rapidly by bluegill sunfish with a total residue bioconcentration factor of 11 x for whole fish.

Aquatic compartment

The 96-hour LC_{50} value for Rainbow trout (*Salmo gairdneri*) was 53 mg/l with 95% confidence limits of 45-63 mg/l. The acute toxicity test for *Daphnia magna* resulted in a 48 h-EC_{50} of > 14 mg/l (maximum measured tested concentration). The effect of coumatetralyl on the of growth rate of green alga *Scenedesmus subspicatus* was characterised with an E_rC_{50} value of > 18 mg/l after 72 h. Due to the low toxicity to bacteria the self cleaning potential of surface waters is not endangered.

For *Oncorhynchus mykiss* a 21-d NOEC of 5.0 µg/l was determined, the LOEC was 15.8 µg/l. The prolonged acute NOEC of 5.0 µg/l is used in the risk assessment for the aquatic compartment. The chronic NOEC (21 days) for *Daphnia magna* was determined to be 0.10 mg/l, the LOEC was 0.32 mg/l.

Therefore, classification/labelling for acute toxicity should be R52/53: Harmful to aquatic organisms may cause long-term adverse effects in the aquatic environment.

Terrestrial compartment

Coumatetralyl shows only a low acute toxicity to earthworms (*Eisenia foetida*). The LC_{50} at 7 and 14 days was calculated to be nominally 225 mg/kg dry weight soil. In acute and subacute tests with Japanese quail (*Coturnix coturnix japonica*) Coumatetralyl shows also only a low acute avian toxicity. The acute test revealed an LD_{50} of > 2000 mg a.i./kg bw. No mortalities were observed in the controls and in the treated groups. The NOEL of 500 mg a.i./kg bw was based on clinically observed signs of toxicity. The 5-day sub-acute dietary test with Japanese quail resulted in an LC_{50} of 1733 mg a.i./kg feed. As discussed and agreed with the RMS an avian reproduction study performed in accordance with the new OECD test guideline was done. When looking at specific reproductive endpoints, the NOEC is 60 mg a.s./kg food. However, based on observed mortality and findings at gross necropsy the NOEC for parental toxicity is 20 mg a.s./kg food and this value will be used for the Risk Assessment.

PNEC calculations

In surface waters

According to TGD for Risk Assessment (2003), when three chronic toxicity NOECs are available from at least three species across three trophic levels (as fish + daphnid + algae) an assessment factor of 10 applies to the lowest of three long-term NOECs. However, as the fish test only can be considered as a long term test/prolonged acute test a assessment factor of 50 is applied to the trout 21 day NOEC = 0.005 mg a.i./l

With chronic toxicity data: PNECwater = 5 µg/l / 50

= 0.1 µg/l

In Sewage Treatment Plants (STP):

According to TGD for Risk Assessment (2003), considering the EC50 toxicity data from an activated sludge study, an assessment factor of 100 applies

For STP scenario: $PNEC_{STP}$. = 4210 mg/l / 100

= 42.1 mg/l

PNEC sediments:

Since both the PNEC and the PEC values for sediment only can be calculated using the equilibrium method, the risk to the sediment will be the same as described for surface water. Therefore the risk of the sediment will not be considered further.

PNEC soil:

The data set for coumatetralyl contains only one study with soil organisms (acute earthworm, LC_{50} = 225 mg/kg dry weight soil). According to TGD for Risk Assessment (2003) results from short-term studies with soil organisms are divided by an assessment factor of 1000 to calculate the PNECsoil:

PNECsoil = 225 mg/kg dry weight soil / 1000

= 0.225 mg/kg dry weight soil.

Calculation of PNEC using the equilibrium partitioning method

PNECsoil = 9.3/1500 x 0.1111 x 1000

= 0.0006 mg/kg dry weight soil

The PNEC via EPM is much lower than the one derived from the earthworm test. According to the TGD the EPM may not be suitable for lipophilic compounds or substances with a specific mode of action nor for species that are exposed primary through food. Furthermore, this approach does not consider the effects on soil organisms of chemicals that are adsorbed to soil particles and taken up by ingestion. For coumatetralyl, which has a specific mode of action and where the species are primarily exposed through food, the EPM seems not to be a suitable method and the terrestrial risk assessment will be based on the PNECsoil of 0.225 mg/kg dry weight soil derived from the earthworm test. Furthermore, the applicant will not be asked to submit a soil micro-organisms or a plant test because the RMS do not think that such tests will change the decision of the effect assessment for the terrestrial compartment do the the specific action of the antianticouagulants.

PNEC of non-target mammals and birds (secondary poisoning)

Birds:

The toxicity of birds is documentet by acute and long-term studies. The basic set of data requirements is thus fulfilled. The chronic reproduction toxicity study with a NOEC of 20 mg a.i./kg food, corresponding to 2 mg a.i./kg bw is used for the PNEC calculations. An AF of 30 is used for these calculations

$PNEC_{oral}$ = 20 mg a.i./kg food /30 = 0.667 mg a.i./kg food corresponding to 0.0667 mg a.i / kg bw.

Mammals:

For the NOEC calculation of mammals the NOEC from the subchronic oral toxicity test in rats (feeding study for 16 weeks) is used:

NOEC (90 days) = 13 mg a.s./kg food and a NOAEL of 0.0068 mg a.s. / kg bw/day.

For the PNEC calculations an AF of 90 is used.

$PNEC_{oral}$ = 0.14 mg a.i. /kg food

or

$PNEC_{oral}$ = 0.0001 mg a.i. /kg bw.

2.2.2.2. Environmental exposure and risk assessment

Exposure scenarios are defined for sewer system, in/around building, in the open area and waste dumps with sewage treatment plant (STP), surface water and soil as the relevant exposed environmental compartment. Racumin® Paste is a ready to use bait which resembles a highly viscous, dough-like log. Unlike wax blocks, there are no cereal grains contained in the product. The paste comes in 10 and 100 gram units, with the recommended quantity placed in a single bait box or non-accessible area being 200 grams (2 large units). In addition, unlike any other

product type described in EUBEES ESD 2003, the paste product is never handled in a loose form during application; it is enclosed in a paper sachet which is not removed.

Exposure for sewer system

If coumatetralyl is applied in sewer systems, the STP will be the major exposed environmental compartment. Due to the rapid metabolism of coumatetralyl in the body of rats, the indirect release of active compound and its main metabolite to environment is limited. The realistic worst case scenario is based on a default sewage treatment plant from 10,000 person equivalent according to TGD for risk assessment and the following assumption: On day 1, 300 Racumin paste blocks are applied to 300 cesspools in an area corresponding to 10,000 PE, on day 7, at a revisit 100 paste blocks are eaten and therefore replenished, then on day 14 at a revisit only 50 paste units have been eaten and are replaced. Maximum coumatetralyl emission during first week 100 paste units (= 10 kg bait).

In a realistic worst case scenario the PEC/PNEC of 0.000005 and 0.21 for coumatetralyl and its major metabolite were calculated for the STP compartment and in surface water respectively (with an extremely conservative assumption that the metabolite toxicity is the same as parent). Based on these results, a risk of coumatetralyl treatment in sewage systems for STP and surface water can be excluded.

Exposure in or around buildings

The main exposure of environment is expected to be soil contaminated by spills during application, refilling and disposal operations. The exposure to STP is considered negligible for the application of coumatetralyl paste formulation. The first scenario for application in and around building is 21-days treatment campaign using 10 bait stations filled with 200 g paste per box on day 1 (typical for Racumin treatment) and completely replenished 4 times on day 3, 7, 14 and 21 since it is assumed that all of the paste has been eaten. The estimated direct release during application and use is 1 %. Based on very conservative first step worst case assumptions (paste replenished completely five times during a campaign of 21 days, 90 % disperse release of coumatetralyl via urine and faeces) a PEC/PNEC of 0.14 was determined. Even with an extremely conservative assumption that the metabolite toxicity is the same as parent. Furthermore, the calculations are related only to the “hot spot” regions directly (up to 10 cm) around the bait stations. Therefore no significant risk of coumatetralyl treatment to the soil environment is expected.

Exposure scenario for waste dumps

The soil is potentially exposed by rodenticide residues after treatment while exposure of rodenticide residues to STP after application on waste dumps is not relevant. According to EUBEES ESD (2003) most of the bait is eaten and returned to soil as urine, faeces and dead animals.

Based on the low PEC/PNEC relations for a conservative worst case (PEC/PNEC = 0.247) a risk for the soil compartment due to the use of coumatetralyl as a rodenticide in waste dumps is not expected.

Exposure scenario for Open Areas

Based on a Tier 1 assumption a PEC/PNEC of 10.44 was determined for the realistic worst case scenario. However, the calculation are related only to the “hot spot” regions directly (up to 10 cm) around the bait hole and do not take into consideration the biodegradation of coumatetralyl in soil. In tier II we first take into account the biodegradation in soil and then a PEC/PNEC of 0.65 is found in the “hot Spot” regions directly around the bait holes after 4 month. If we increase this area to e.g. 20 cm then the PEC/PNEC ratio will be even lower.

Non compartment specific effects relevant to food chain

Certain non-target animals are potentially at risk from rodenticides by eating Racumin Paste or rodents that have taken up/accumulated the poison. The calculation schemes (tier 1 and tier 2) introduced in EUBEES ESD (2003) and Addendum relevant to Biocides to the TGD on Risk Assessment (Endorsed at the 23rd CA meeting Nov. 2006) for the characterization of primary and secondary poisoning effects of rodenticides both indicate a risk. However, the limitations and uncertainties of the assumptions used in the calculations are obvious and are also discussed in EUBEES ESD (2003). An extremely high assessment factor, which must be applied to the PNEC, is most responsible for the conservative calculation results.

It can be concluded that Racumin® Paste may pose a potential risk to non-target species with respect to primary poisoning in the realistic worst case scenario. However, Racumin® Paste is likely to exert some avoidance to birds and mammals and therefore not pose an unacceptable risk with respect to primary poisoning compared to other formulations of rodenticides. However, accidental risk of primary poisoning of non-target animals cannot be excluded.

The calculation schemes (tier 1 and tier 2) introduced in EUBEES ESD (2003) and Addendum relevant to Biocides to the TGD on Risk Assessment (Endorsed at the 23rd CA meeting Nov. 2006) for the characterisation of secondary poisoning effects of rodenticides both indicate a risk of secondary poisoning. The results of several field and laboratory studies with different warm-blooded species which were performed with coumatetralyl also indicate a potential risk at a realistic worst conditions. However, in these investigations the animals were fed exclusively with poisoned rodents over longer time periods (portion of diet (PD) = 1). As is pointed out in EUBEES ESD (2003) predators and scavengers may have very large hunting areas, and these hunting areas may cover several times the areas that had been treated with an anticoagulant rodenticide. Therefore a realistic portion of diet will be much lower than 1 ($PD \leq 0.5$). According to the review of Joermann (1998), the use of first-generation anticoagulants presents a lower hazard potential to birds than to other non-target mammals.

With regard to the observed potential risk of pets (dogs and cats) from eating rats which were poisoned with coumatetralyl or wild mammals (like ferret), the use of the rodenticide must be performed according to the product instructions. Poisoned rats that have died away from cover on the surface must be collected immediately and deposited correctly to avoid any exposure to non-target animals. During treatment campaigns dogs and other pets should not have access to areas near bait stations and poisoned rats. If the rodenticide application is done correctly, exposure to pets happens only accidentally.

Conclusion – Qualitative risk assessment for acute situation

Primary poisoning

It appears that among the non-target mammals, dog is the species most sensitive to coumatetralyl after a single oral dose with a value of LD50 = ~35 mg/kg bw (bw: body weight). In general, the effect dose for acute toxicity to rats after a single oral dose is lower than for non-target mammals with values of LD50 in the range 5-30 mg/kg bw, while mice seem to be considerably more tolerant (LD50 = 2,000 – 4,000 mg/kg bw) (Andrews 1999). The tested species of birds are considerably less sensitive than the mammals with LD50 > 2,000 mg/kg bw.

Accidental poisoning of dogs is also unlikely if product is used appropriately. However, even if an animal eats 2 X 100 gram sachets, the maximum applied in any one place, death is unlikely (dose level ~20% of the LD50).

However, it must be stressed that that this qualitative assessment is not intended to be used for the risk assessment of primary poisoning of rodenticides. The comparison only gives a first indication of the acute toxicity of the substance. The conclusion of this comparison should NOT be that the substance is not acutely toxic or "unproblematic" with regard to the acute primary poisoning situation because a comparison is made with a single dose LD50 without applying an assessment factor.

Secondary poisoning

Based on the present quantitative description where the toxicity of the substance is compared to the possible single uptake no indication of a significant lethal toxicity was demonstrated. However, it must be stressed that this quantitative assessment is not intended to be used for the risk assessment of secondary poisoning of rodenticides. The comparison only gives a first indication of the acute toxicity of the substance. The conclusion of this comparison should NOT be that the substance is not acutely toxic or "unproblematic" with regard to the acute secondary poisoning situation because a comparison is made with a single dose LD50 without applying an assessment factor. Furthermore, it should be noted that as described in the TGD some specific considerations need to be made for the use of the assessment factor for predators. The protective value of the "normal" interspecies variation factor may be questionable in case of predators. On top of that, many predator species are characterised by typical metabolic stages in their life-cycle that could make them extra sensitive to contaminants.

Conclusion – Qualitative risk assessment for long-term situation

It can be concluded that Racumin® Paste poses an unacceptable risk to non-target species with respect to primary poisoning in the realistic worst case scenario. However, Racumin® Paste is likely to exert some avoidance to birds and mammals and therefore not pose an unacceptable risk with respect to primary poisoning compared to other formulations of rodenticides. However, accidental risk of primary poisoning of non target animals cannot be excluded.

Experimental data of primary poisoning of non-target organisms

The results of the non-taget bird and mammal primary poisoning calculations suggest a level of risk exists. However, results from several available feeding studies are available which should be taken into account.

The assessment of the potential for primary poisoning of non-target organisms consists of an assessment of the possible intake of coumatetralyl and the potential effects of this intake. Ideally, the risk of primary poisoning should be assessed for any non-target species that may be exposed. However, effect data are available only for a few non-target mammals and birds and only for studies with rabbit and Japanese quail are study summaries submitted in the dossier.

The repeated dose toxicity tests referred show that the mammals tested are very sensitive to repeated doses of coumatetralyl with full mortality at an estimated total intake of between 1 and 2 mg a.i./kg bw (a.i.: active ingredient) for dog and pig within a period of 7 days, and a LD50 < 1 mg a.i./kg bw for rabbit within a 28-days period. In a 28-days reproduction toxicity study with rabbits, a NO(A)EL at 0.0125 mg a.i./kg bw*day was determined corresponding to a total intake of 0.26 mg a.i./kg bw. These results correspond to an estimated concentration in food of 6-10 mg a.i./kg food for the mortality studies and 0.42 mg/kg food in the reproduction study. Birds are considerably less sensitive than mammals and hens are the most sensitive species among the birds with an estimated LD50 at a total intake of ~80 mg a.i./kg bw through 15 days corresponding to an estimated concentration in food of ~43 mg a.i./kg food.

secondary poisoning

The calculation schemes (tier 1 and tier 2) introduced in EUBEES ESD (2003) for the characterisation of secondary poisoning effects of rodenticides both indicate a risk of secondary poisoning. It is considered that the proposed scenarios are conservative. The limitations and uncertainties of the assumptions used in the calculations are obvious and are also discussed in EUBEES ESD (2003). According to EUBEES ESD (2003, p. 45) “there is an element of uncertainty if $PNEC_{oral}$ calculated according to the TGD is really very suitable for rodenticides”

High assessment factors which must be applied to the PNEC are most responsible for the conservative calculation results.

However, the results of several field and laboratory secondary poisoning studies with different warm-blooded species, which were, performed with coumatetralyl also gives information on a potential risk.

In the mentioned studies on barn owl, kestrel and weka no mortalities were observed. In these investigations the birds were fed exclusively with poisoned rodents (normally exposed to the rodenticide for 3 days) over 3-6 days for barn owl and kestrel and for op to 4 weeks for kestrel (portion of diet *(PD)* = 1). For the long term exposure with kestrel internal haemorrhages of increasing intensity with increasing exposure of mice was seen. As is pointed out in EUBEES ESD (2003) predators and scavengers may have very large hunting areas, and these hunting areas may cover several times the areas that had been treated with an anticoagulant rodenticide. Therefore a realistic portion of diet will be much lower than 1 ($PD \leq 0.5$). According to the review of Joermann (1998), the use of first-generation anticoagulants presents a lower hazard potential to birds than to non-target mammals.

In the mammalian investigations with dog and ferret, mortalities and relevant toxic effects were only found under realistic worst-case conditions. With regard to the observed potential risk of pets (dogs and cats) from eating rats which were poisoned with coumatetralyl or wild mammals (like ferret), the use of the rodenticide must be performed according to the product instructions. Poisoned rats which have died away from cover on the surface must be collected immediately and deposited correctly to avoid any exposure to non-target animals. During treatment campaigns dogs and other pets should not have access to areas near bait stations and poisoned rats. If the rodenticide application is done correctly, exposure to non-target mammals and birds happens only "accidentally".

2.2.3. Compliance with the criteria for approval of active substance according to Annex VI of directive 98/8/E*C.*

The approval criteria of Annex VI of Directive 98/8/EC are further explained in Technical Notes for Guidance on Annex I Inclusion.

All health and environmental criteria of approval are fulfilled except for accidental exposure of infants and primary and secondary poisoning where unacceptable risks are found. The risk of accidental exposure of infants should be addressed by implementation of risk reduction measures listed in point 3. With the exception of the primary and secondary poisoning there are no unacceptable effects on the environment when risk mitigation measures listed under point 3 are adopted. Under the proposed conditions of use coumatetralyl fulfils the following health and environmental criteria for approval with the exception of the accidental exposure of infants and primary and secondary poisoning issue:

- The criteria for approval with respect to PEC/PNEC ratio in soil, surface water and sediment
- The criteria for approval with respect to behaviour in soil
- The criteria for approval with respect to behaviour in water/sediment
- The criteria for approval with respect to ground water (the maximum permissible concentration laid down by Directive 80/788/EEC as amended by 98/83/EC) is not assumed to be a issue under the proposed conditions of use.
- The criteria for approval with respect to bioaccumulation
- Coumatetralyl do not fulfil the PBT- or vPvB criteria.
- The criteria for restricted uptake on Annex I of the substance, as the product is not classifiable in any of the criteria excluding such an uptake

2.2.4. 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 evaluation of coumatetralyl, for use in product type 14 (rodenticides), is that it may be possible for Member States to issue authorisations of products containing coumatetralyl in accordance with the conditions laid down in Article 5 of Dir. 98/8/EC.

Rodent control is needed to prevent disease transmission, contamination of food and feeding stuffs and structural damage. It is recognised that anticoagulant rodenticides may cause pain in rodents but it is considered that this is not in conflict with the requirements of Art. 5.1 of the BPD 'to avoid unnecessary pain and suffering of vertebrates', *as long as effective, but comparable less painful alternative biocidal substances or biocidal products or even non-biocidal alternatives are not available.*

Assessed from the documentation for the active substance, coumatetralyl, and the representative product, Racumin®Paste, biocidal products intended to control rats may be sufficiently effective and without unacceptable effects to human health of the users. It is recognised that anticoagulant rodenticides may cause risk of both primary and secondary poisoning for non target animals and may pose a risk to young children if accidentally ingested and according to the critieria and guidance of the directive 98/8/EC, this substance should not normally be included in Annex I. However, the RMS believes that it is important to have a range of active ingredients for use in rodenticides in the EU in the interest of public health and hygiene. Therefore, the RMS recommends coumatetralyl for inclusion into Annex I. However special precautions must be taken in order to avoid unacceptable resistance to the anticoagulant as well as it is of paramount importance that exposure to humans and non-target animals is minimised by relevant risk mitigation measures.

This conclusion relies on the fact that users of the biocidal product will be applying the basic principles of good practice and respect the conditions for the use recommended on the label of the product.

Coumatetralyl is a candidate for a comparative risk assessment due to the risk posed to birds and mammals. Such a comparative assessment can only be performed when possible alternative rodenticides have been evaluated.

3.2. Decision regarding the inclusion on to Annex I

The Danish CA recommends that coumatetralyl is included in Annex I of the Directive 98/8/EC as an active substance in rodenticides (Product Type 14), subject to the following specific provisions according to Article 10(2)(i)(a-f) of Dir. 98/8/EC:

a) The active substance coumatetralyl, as manufactured, shall have a minimum

purity of ≥ 98% w/w

b) The identity and maximum content of impurities must not differ in such a way as to invalidate the assessment for the inclusion of the active substance on Annex I

c) Primary as well as secondary exposure of humans, non-target animals and the environment are minimised by considering and applying all appropriate and available risk mitigation measures, These include, amongst other, the restriction to professional use only, setting an upper limit to the package size and laying down obligations to use tamper resistant and secured bait boxes.

3.3. Justification for the provisions regarding the inclusion on to Annex I

a) and b) are general requirements that will be obligatory specification demands for the active substance for all Annex I-entries.

c) Important toxicological core data requirements have been waived in the evaluation procedure because it was justified that exposure to humans and animals thereby could be minimised to an acceptable level. Furthermore, a risk was identified for both humans and the environment. For humans, a risk was identified for infants through accidental exposure and for the environment for non-target organisms from primary- and secondary exposure. Therefore, controlled, protected application is necessary to secure safe use.

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

- The risk assessment in this evaluation was based on information focused on a specific representative product, Racumin®Paste, formulated as a paste in small paper sachets and the evaluation showed that this product has advantages over other types of formulations. Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Article 5(1) and of the common principles laid down in Annex VI to Directive 98/8/EC.

- Risk mitigations measures like the use of a aversive agent and a dye to the biocidal product and, when appropriate, use of a special formulation, e.g. a paste, or restrictions regarding formulation type e.g. tracking powders, should be elements to be taken into account by Member States when authorising products. These should be applied in a manner consistent with earlier decisions taken regarding other active substances in PT 14.

In addition to the elements already listed in Article 20(3) of Directive 98/8/EC, all packaging of anticoagulant rodenticides should be marked with the following standard phrases to project humans, animals or the environment:

- Baits must be securely deposited in a way so as to minimise the risk of consumption by other animals or children. Where possible, secure baits so they cannot be dragged away.

- Search for and remove dead rodents at frequent intervals during treatment (unless used in sewers), at least sa often as when baits are checked and/or replenished. Dispose of dead rodents in accordance with local requirements.

- Remove all baits after treatment and pispose of them in accordance with local requirements

- Keep out of the reach of children

This last safety precaution should always be carried on the lable of the products, if not already legally required by Directive 1999/45/EC. The others could be stated elsewhere on the packaging or on an accompanying leaflet together with the other directions for use and disposal of the product required by article 20(3) of directive 98/8/EC.

Member States should encourage the application of Codes of Good Practices in rodent control. These measures could include (but should not be restricted to) the following factors:

- The population size of the target rodent should be evaluated before a control campain. The number of baits and the timing of the control campaign should be in proportion to the size of the infestation.

- A complete elimination of rodents in the infested area should be achieved.

- The use instruction of products should contain guidance on resistance management for rodenticides.

- Resistant management strategies should be developed, and coumatetralyl should not be used in an area where resistance to this substance is suspected.

- The authorisation holder shall report any observed resisttance incidents to the Compentent Authorities or other appointed bodies in resistance management.

- When the product is being used in public areas, the areas treated must be marked during the treatment period and a notice explaining the risk of primary or secondary poisoning by the anticoagulant as well as indication the first measures to be taken in case of poisoning must be made available alongside the baits.

3.5. Requirement for further information

The information and justifications supplied in accordance with Annex II and Annex III of Dir. 98/8/EC have been accepted as sufficient to recommend the inclusion of coumatetralyl on to Annex I.

The following studies or information should be submitted when the applying for authorisation of a biocidal product containing coumatetralyl for the first time after Annex I inclusion of the active substance:

a) Confirming calculation of the value for the partition coefficient.

b) Due to possible accidental or deliberate contamination, an analytical method for residues in/on food or feedstuffs

c) Validation data for the method of analysis for one of the impurities specified in document IIA, confidential part.

3.6. Updating this Assessment Report

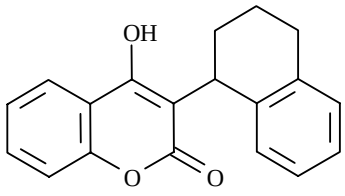
This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information referred to in Articles 7, 10.4 and 14 of Directive 98/8/EC. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the inclusion of coumatetralyl 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)	3-(alpha-tetralyl)-4-hydroxycoumarin
Function (e.g. fungicide)	Rodenticide
Rapporteur Member State	Denmark

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	4-hydroxy-3-(1, 2, 3, 4-tetrahydro-1-naphthyl)coumarin
Chemical name (CA)	2H-1-benzopyran-2-one, 4-hydroxy-3-(1, 2, 3, 4-tetrahydro-1-naphthalenyl)
CAS No	5836-29-3
EC No	227-424-0
Other substance No.	CIPAC N° 189
Minimum purity of the active substance as manufactured (g/kg or g/l)	> 980 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Confidential information see Document IIIA- confidential data
Molecular formula	$C_{19}H_{16}O_3$
Molecular mass	292.3 g/mol
Structural formula	

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

Melting point (state purity)	168.8 °C (Purity : 98.8%)
Boiling point (state purity)	no boiling point
Temperature of decomposition	195°C
Appearance (state purity)	White to yellow-grey crystalline powder (Purity 99.96 %)
Relative density (state purity)	1.328 at 20°C (Purity : 98.8%)
Surface tension	73.08 mN/m at 20 °C and 4.383 mg/L (90% saturation)
Vapour pressure (in Pa, state temperature)	< 1.0E-03Pa (20 °C); A more precise extrapolated value at 20°C is lacking.

Henry's law constant (Pa m^3 mol^{-1})	K < 6,64.10-2 Pa.m3.mol-1
Solubility in water (g/l or mg/l, state temperature)	Not buffered water pH 5.1: 4.40E-03 g/l at 20 °C pH5: 4.78E-03 g/l at 20 °C pH9: 4.65 g/l at 20 °C pH7: 4.60E-01 g/l 20 °C,
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	Measured at 20°C 2-Propanol: 16.4 g/l, Dichlormethane: 44.3 g/l, Xylene: 2.7 g/l, Polyethylenglycol: 37.9 g/l Acetone: 25.4 g/l, Ethylacetate: 11.8 g/l, Acetonitrile: 6.8 g/l, Dimethylsulfoxide: >250 g/l Cyclohexanone: 80.9 g/l, Toluene: 3.9 g/l
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	The active substance as manufactured didn't include any organic solvent.
Partition coefficient (log P_{OW}) (state temperature)	demineralised water Log P_{ow} (pH 5.8) = 2.95 pH5: 3.4 at 20 °C pH7: 1.5 at 20 °C pH9: -0,1 at 20 °C,
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	pH 4 Hydrolytically stable pH 7 Hydrolytically stable pH 9 Hydrolytically stable
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	pK-value in water/acetone = 5.3
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	271 nm: ε 11769 282 nm: ε 12059 308 nm: ε 10623
Photostability (DT_{50}) (aqueous, sunlight, state pH) (point VII.7.6.2.2)	Aqueous : Coumatetralyl was degraded rapidly by light to a number of degradation products, of which salicylic was identified as a major product. Due to lack of information, no exact conclusion regarding possible degradation rate (half-life) can be drawn. However, the results indicate a short half- life (a few hours to one day).

Quantum yield of direct phototransformation in water at Σ > 290 nm (point VII.7.6.2.2)	n.a
Flammability	not highly flammable
Autoflammability	No self-ignition up to the melting point at 168.8°C
Explosive properties	No explosive properties
Oxidising properties	Not oxidising

Summary of intended uses

Product Type	Field of use envisaged	Likely conc., at which a.s. will be used
PT 14 Rodenticide	Product is used to control rodents, especially rats in sewage systems, in and around buildings and on waste dumps	0.0375 % coumatetralyl in paste formulation

Proposed classification and labelling of a.s (Annex IIA, point IX.)

with regard to physical/chemical data		
with regard to toxicological data	T+	Very toxic
	R61	May cause harm to the unborn child
	R 26/28	Very toxic by inhalation and if swallowed.
	R 24	Toxic in contact with skin
	R 48/23/24/25	Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.
with regard to fate and behaviour data	None	
with regard to ecotoxicological data	R52/53	Harmful to aquatic organisms may cause long-term adverse effects in the aquatic environment

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	After extraction, an aliquot is injected into the HPLC with reversed-phase separation using isocratic elution and with a UV detection at 310 nm. The coumatetralyl concentration is determined using external standardization.
Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	Reverse-phased-HPLC, uv-detection, GC-FID, ion-exchange chromatography with electrical conduction and titration are the principles of the analytical methods used for determination of impurities in the technical substance

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	After extraction of soil samples with mixtures of water / acetonitrile, subsamples of extracts are identified and quantified by HPLC using MS/MS detection in the Multiple Reaction Monitoring mode. The limit of quantification is 1 µg/kg for coumatetralyl.
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Air is drawn through the adsorption tubes containing active substance with a rate of 2 l/min during a period of six hours. The adsorbed active substance is extracted with acetonitrile and determined by liquid chromatographic separation using UV detection (DAD) with an external standard. The limit of quantification was 0.030 mg coumatetralyl/m^3 air
Water (principle of method and LOQ) (Annex IIA, point 4.2)	Water samples are analysed by direct injection into an HPLC instrument with electropray MS/MS-detection.. Coumatetralyl content is determined using external standardization. The limit of quantification for coumatetralyl is 0.05 µg/l.
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	Coumatetralyl in animal liver tissue is determined using a HPLC with fluorescence detection. A post-column pH switching technique using ammonia/methanol/water exploits the natural fluorescence of this compound. Warfarin is used as an internal standard. The method detection limit (MDL) in tissue is 0.1 mg/kg, where the tissue sample weighs 2 g.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	n.a
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	n.a.

Chapter 3: Impact on Human Health

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

Rate and extent of oral absorption:	Orally absorbed fraction of at least 75% and 86% of single oral dose (males and females, respectively). Oral absorption of 75% used for risk assessment.
Rate and extent of dermal absorption:	**Rats, 8 hour in vivo exposure:** 4.44%, 5.26%, 3.47%, and 4.47% of applied dose at 8, 24, 72 and 168 hours post-application, respectively. Rats: 8 hr in vitro exposure: 1,44% at 24 hrs Human 8 hr in vitro exposure : 0.316% at 24 hrs, exposure 1.14% Human dermal absorption derived value: 1.14%
Distribution:	Single dosage,rats: 49 – 56% retained in body. Repeated dosage: 18% retained. Liver (21 –25% after single treatment and 7% after repeated dosing), Skin (7-16% after a single dose and 4% of the dose after multiple dosing). All other organs retained less than 1% of the dose at sacrifice.
Potential for accumulation	The radioactivity remaining in the body of the rat after 7 days was 49-56%, after repeated exposure decreased to 18%. The site of accumulation is the liver, however the rate of excretion from the liver is not known.
Rate and extent of excretion:	Slow excretion, dependent on sex and on the number of applications (single dose or repeated dose). Single-dosed males excreted about 20% of the administered dose with the urine and about 20% with the faeces until sacrifice (7 days post administration). After repeated dosing the ratio shifted towards 44% renal and 33% faecal excretion until sacrifice. Single-dosed females excreted about 37% with the urine and about 12% with the faeces until sacrifice. Excretion of coumatetralyl in the exhaled air was negligible, i.e. less than 0.60% of the administered dose.
Toxicologically significant metabolite	One main metabolite (13-hydroxy-coumatetralyl, MT0315A) accounted for up to 27% of the applied dose. Additionally, three isomers of the main metabolite were detected, all far below 10% of the dose. In urine two further metabolites could be verified (both approx. 2%).

Acute toxicity (Annex IIA, point 6.1)

Rat LD_{50} oral	Rat male (fasted): 30 mg/kg bw Rat female (fasted): approximately 15 mg/kg bw
Rat LD_{50} dermal	Rat males: 100 < LD50< 500 mg/kg bw

	Rat females: 258 mg/kg bw
Rat LC_{50} inhalation	Male: approx. 0.063 mg/l/4h Female: approx. 0.039 mg/l/4h
Skin irritation	Non-irritant
Eye irritation	Non-irritant
Skin sensitization (test method used and result)	Non-sensitiser in a Buehler Patch test

Repeated dose toxicity (Annex IIA, point 6.3)

Species/ target / critical effect	The critical effect of coumatetralyl observed in all studies is the effect on blood coagulation withhaemorrhage and prolonged blood clotting time
Lowest relevant oral NOAEL / LOAEL	0.0068 mg/kg bw/day(16 weeks, rat
Lowest relevant dermal NOAEL / LOAEL	Not performed
Lowest relevant inhalation NOAEL / LOAEL	Not performed

Genotoxicity (Annex IIA, point 6.6)	In vitro tests negative. Coumatetralyl is unlikely to be genotoxic

Carcinogenicity (Annex IIA, point 6.4)

Species/type of tumour	Study waived.
lowest dose with tumours	Unlikely to be carcinogenic

Reproductive toxicity (Annex IIA, point 6.8)

Species/ Reproduction target / critical effect	Study waived
Lowest relevant reproductive NOAEL / LOAEL	
Species/Developmental target / critical effect	Rat: bleedings, symptoms of anaemia and mortality in dams Rabbit: internal and external bleedings and mortality in dam
Lowest relevant developmental NOAEL / LOAEL	Rat : NOAEL / LOAEL maternal toxic effects : LO(A)EL = 0.070 mg/kg bw ; NO(A)EL = 0.035 mg/kg bw NOAEL / LOAEL Embryotoxicity and/or foetotoxicity: NO(A)EL = 0.14 mg/kg bw (LO(A)EL n.a) NOAEL / LOAEL Teratogenicity: NO(A)EL = 0.14 mg/kg bw (LO(A)EL n.a) Rabbit : NOAEL / LOAEL maternal toxic effects : LO(A)EL = 0.025 mg/kg bw ; NO(A)EL = 0.0125 mg/kg bw NOAEL / LOAEL Embryotoxicity and/or foetotoxicity :

	LO(A)EL = 0.05 mg/kg bw ; NO(A)EL = 0.025 mg/kg bw NOAEL / LOAEL Teratogenicity : NO(A)EL = 0.05 mg/kg bw (LO(A)EL n.a)

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

Species/ target/critical effect Lowest relevant developmental NOAEL / LOAEL.	n.a

Other toxicological studies (Annex IIIA, VI/XI)

Sub-chronic oral toxicity study (112 d) on Racumin 0.75% tracking powder	Rat : NOAEL (males) = 0.0068 mg/kg bw/day NOAEL (females) = 0.0083 mg/kg bw/day

Medical data (Annex IIA, point 6.9)

.....	During the production period of more than 20 years up to the year 2002 no accidents with coumatetralyl were registered in the Medical Department and no consultations due to contact with coumatetralyl were required From 1994 to 2003, 35 complaints/adverse incidents from Germany concerning products containing coumatetralyl were recorded. Of these, 17 were requests for information, among these 7 attempted suicides, and two alleged poisoning by others. In 8 cases, the product had been swallowed accidentally (max. 40 g) without any symptoms occurring. Two further cases were symptomatic: an adult showed a slight coagulation inhibition following oral absorption of two teaspoons of Racumin Plus and a child having ingested an unknown amount and required vitamin K1 therapy. No sequelae occurred. In seven cases, contact with eyes or skin had occurred, either by accident or by lack of personal protective equipment (e.g. distributing the powder with bare hands). In five cases, symptoms were reported. Three affected persons showed short-term nausea, one showed swelling and itching of the hands after washing, and in one subject irritation of the eyes occurred. The irritation is regarded as due to the product (definite correlation), the skin reaction as possible, and the nausea as unlikely but it is most probably a secondary reaction to the fear of being poisoned

Summary (Annex IIA, point 6.10)	Value	Study	Safety factor
ADI (if residues in food or feed)	n.a		
$AEL_{subchronic}$ AOEL	0.017 µg/kg	Subchronic oral	300 (default AF

	bw/day	exposure of male rats	of 100, extra factor of 3 for severity of developmental effect and correction factor of 0.75 for limited oral absorption)
Drinking water limit	n.a		
AEL_{acute}	0.031µg/kg bw/day	Developmental toxicity study in rabbits	300 (default AF of 100, extra factor of 3 for severity of developmental effect and correction factor of 0.75 for limited oral absorption)

Acceptable exposure scenarios (including method of calculation)

Professional users	Application scenario: spearing bait sachets onto wire for the placement in e.g. sewers Disposal scenario: removing of bait sachets from wire they were speared on. Size of the sachets: 100 g per sachet Frequency of daily exposure through application and disposal: 60 bait sachets+ 15 bait sachets (concentration of a.s.:0. 375 g a.s./kg paste) Level of personal protection: gloves are not worn (worst case) and gloves are worn (normal use) when handling the bait sachets. Exposure levels without gloves: 0.011-0.15 µg/kg bw/day With gloves: 0.000067-0.00044µg/kg bw/day. Acceptable risk: 0.39-87.6% of AEL, MOE: 340-76000
Non-professional users	Application scenario: placing bait sachets into e.g. bait boxes Disposal scenario : removing bait sachets out of e.g. bait boxes Size of the sachets: 100 g per sachet Frequency of application: 5 bait sachets per day (0.5 kg Racumin® Paste per day) Frequency of disposal: 3 bait sachets per day (2 are partly eaten by rats) Concentration of a.s.:0. 375 g a.s./kg paste Level of personal protection: no gloves worn. Exposure levels:0.000086-0.00028 µg/kg bw/day. Acceptable risk: 0.5-1.6% of AOEL, MOE: 18400-59000

Indirect exposure as a result of use	Transient mouthing/infants ingesting 10 mg (TNsG on Human Exposure, default value for bait treated with repellent. Acceptable risk: 0.1% of AEL_{acute} . MOE: 250000. Child eating a bite of bait: 5g (User Guidance to TNsG on Human exposure- default value). Unacceptable risk: 612% of AEL_{acute}, MOE:50. Risk reduction measures as addition of bittering agent and use of bait station expected to reduce risk to acceptable level.

Chapter 4: Fate and Behaviour in the Environment

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 4 Hydrolytically stable
	pH 7 Hydrolytically stable
	pH 9 Hydrolytically stable
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Coumatetralyl was degraded rapidly by light to a number of degradation products, of which salicylic was identified as a major product. Due to lack of information, no exact conclusion regarding possible degradation rate (half life) can be drawn. However, the results indicate a half-life of a few hours to one day.
Readily biodegradable (yes/no)	No
Inherent (yes/No)	No
Biodegradation in seawater	n.a
Non-extractable residues	n.a
Distribution in water / sediment systems (active substance)	n.a
Distribution in water / sediment systems (metabolites)	n.a

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

Mineralization (aerobic)	38-44% after one month and 60-61% after one year. The proportion of bound residues was about 30%
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20°C, aerobic):
	DT_{90lab} (20°C, aerobic):
	DT_{50lab} (10°C, aerobic):
	DT_{50lab} (20°C, anaerobic):
	degradation in the saturated zone:
Field studies (state location, range or median with number of measurements)	DT_{50f}:
	DT_{90f}:
Anaerobic degradation	no significant miniralisation
Soil photolysis	n.a
Non-extractable residues	
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	

Soil accumulation and plateau concentration	

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

Ka , Kd	Ka range : 2.14-8,10 cm^3/g
Ka_{oc} , Kd_{oc}	Ka_{oc} range : 71-735 cm^3/g
pH dependence (yes / no) (if yes type of dependence)	Kd range : 6,67-241 cm^3/g
	Kd_{oc} range : 41-426 cm^3/g

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

	DT50 in air of about 2 hours
Direct photolysis in air	n.a
Quantum yield of direct photolysis	n.a
Photo-oxidative degradation in air	Latitude: ..... Season: ..... DT_{50} .....
Volatilization	n.a

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

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

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Salmo gairdneri	ACUTE	LC50 (96 HRS)	53 mg/l
Oncorhynchus mykiss	Prolonged acute	EC_0 (21 D)	5.0 **µg/l**
Invertebrates			
Daphnia magna	acute	EC50 (48 hrs)	> 14 mg/l
	chronic	NOEC (21 D) LOEC (21 d)	0.10 **mg/l** 0.32 **mg/l**
Algae			
Scenedesmus subspicatus	chronic	EC_r50 (72 hrs) NOEC (72 hrs)	>18 mg/l 5.6 mg/l
Microorganisms			
activated sludge	acute	EC50 (24 hrs)	4210 mg/l

Effects on earthworms or other soil non-target organisms

Acute toxicity to …….. (Annex IIIA, point XIII.3.2)	*Eisenia foetida* LC50 (14 days) = 225 mg/kg dry weight soil
Reproductive toxicity to …… (Annex IIIA, point XIII.3.2)	n.a

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

Nitrogen mineralization	n.a
Carbon mineralization	n.a

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	Acute oral : Rat male (fasted): 30 mg/kg bw Rat female (fasted): approx. 15 mg/kg bw
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	LD50 (Japanese quail) > 2000 mg a.i./kg bw
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	5-d subacute dietary (Japanese quail) LC50 =1733 mg a.i./kg feed
Reproductive toxicity to birds	NOEC = 20 mg a.s./kg feed

(Annex IIIA, point XIII.1.3)	

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

Acute oral toxicity	n.a
Acute contact toxicity	n.a

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

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

Bioconcentration (Annex IIA, point 7.5)

Bioconcentration factor (BCF)	whole fish = 11.4 (+2.8) edible parts = 3.32 (+1.20)
Depration time (DT_{50}) (DT_{90})	DT50 = approx. 14.5 hours
Level of metabolites (%) in organisms accounting for > 10 % of residues	No metabolites identified

Chapter 6: Other End Points

none

Appendix II: List of intended uses

Product Type	Field of use envisaged	Likely conc., at which a.s. will be used
PT 14 Rodenticide	Product is used to control rodents, especially rats (*rattus rattus* and *rattus norvegicus*) in sewage systems, in and around buildings and on waste dumps	0.0375 % coumatetralyl in paste formulation

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 (where different from company)** **Company name, Report No., Date,** **GLP status (where relevant), published or not**	**Data protect. claimed**	**Owner**
6.2. /01	Anderson, C. A.	1999	Benzopyranone-[phenyl-UL-14C]coumatetralyl: Investigation of the biokinetic behaviour and the metabolism in the rat Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: MR-524/98, Edition Number: MO-99-000908 Date: 1999-01-15 GLP, unpublished also filed: Appendix 1. /03 also filed: Appendix 2. /02	Yes	BCS
6.2. /02	Anderson, C.; Bornatsch, W.	1998	Benzopyranone-(phenyl-ul-14C)coumateralyl : In-vitro metabolism in subcellular fractions of rat liver Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: MR523/98, Edition Number: MO-03-003981 Date: 1998-10-26 GLP, unpublished	Yes	BCS
6.4.1.1. /01	Andrews, P.; Romeike, A.	1997	Racumin 0.75% tracking powder (c n.: Coumatetralyl) - Study for subchronic oral toxicity in rats (feeding study for 16 weeks) Bayer AG, Wuppertal, Germany Bayer CropScience AG, Report No.: 26470, Edition Number: MO-03-003996 Date: 1997-07-21 GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIA	**Author(s)**	**Year**	**Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not**	**Data protect. claimed**	**Owner**
3.1.3 /02	Anon.	2003	Racumin techn. S Bayer CropScience AG, Report No.: 065599/12, Edition Number: MO-04-002513 Date: 2003-11-25 Non GLP, unpublished	Yes	BCS
4.1. /01	Anon.	2004	Coumatetralyl 189 Publisher:CIPAC Handbook G, Pages:24-31, Report No.: MO-04-001271, Edition Number: MO-04-001271 Method Report No.: CIPAC 189 Non GLP, published	No	
VIII. /01	Anon.	2004	Racumin techn. S Bayer CropScience AG, Report No.: 102000006018, Edition Number: MO-04-002516 Date: 2004-02-23 Non GLP, unpublished also filed: I.1.2. /01	Yes	BCS
4.2.4. /03	Bacher, R.	2007	Validation of an Analytical Method for the Determination and Confirmation of Coumatetralyl in Blood by LC/MS/MS. PTRL Europe Report No.: P606071806 Edition Number: M-288425-01-1 Date: 2007-05-21 GLP, unpublished	Yes	BCS
6.8.1. /01	Becker, H.; Biedermann, K.	1996	Development toxicity study with Racumin in the rabbit RCC, Research and Consulting Company AG, Itingen, Switzerland Bayer CropScience AG, Report No.: R6742, Edition Number: MO-03-004071 Date: 1996-11-27 GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIA	Author(s)	Year	Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not	Data protect. claimed	Owner
6.8.1. /02	Becker, H.; Biedermann, K.	1995	Dose range-finding developmental toxicity study with Racumin in the rabbit RCC, Research and Consulting Company AG, Itingen, Switzerland Bayer CropScience AG, Report No.: R6487, Edition Number: MO-03-004084 Date: 1995-12-08 Non GLP, unpublished	Yes	BCS
6.8.1. /03	Becker, H.; Biedermann, K.	1996	Developmental toxicity study with Racumin in the rat RCC, Research and Consulting Company AG, Itingen, Switzerland Bayer CropScience AG, Report No.: R6741, Edition Number: MO-03-004091 Date: 1996-11-21 GLP, unpublished	Yes	BCS
6.8.1. /04	Becker, H.; Biedermann, K.	1995	Dose range-finding developmental toxicity study with Racumin in the rat RCC, Research and Consulting Company AG, Itingen, Switzerland Bayer CropScience AG, Report No.: R6460, Edition Number: MO-03-004095 Date: 1995-11-13 GLP, unpublished	Yes	BCS
2.6. /01	Bielefeldt, D.	2004	Description of the manufacturing process of coumatetralyl (Racumin) technical ai Bayer Environmental Science, Dormangen, Germany Bayer CropScience AG, Report No.: ENE11183b, Edition Number: MO-04-002384 Date: 2004-02-25 Non GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIA	**Author(s)**	**Year**	**Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not**	**Data protect. claimed**	**Owner**
4.1. /05	Bissinger, H.; Bruecher, K. H.	2001	Oxarin determination in Racumin by HPLC - validation report ZF-DZA Analytic Uerdingen, Krefeld, Germany Bayer CropScience AG, Report No.: 2301-0222901-92, Edition Number: MO-04-000953 Date: 2001-03-15 Non GLP, unpublished	Yes	BCS
4.1. /06	Bissinger, H.; Pohl, U.	1990	Racumin - Acetone, Methanol, Methyl isobutyl ketone, Toluene - Capillary gas chromatographic method Bayer AG, Krefeld, Germany Bayer CropScience AG, Report No.: 2301-0103504-90E, Edition Number: MO-04-001926 Method Report No.: 2301-0103504-90E Date: 1990-09-06 Non GLP, unpublished	Yes	BCS
3.17. /01	Boecker, T.	2004	Coumatetralyl (Racumin S technical) - Statement on container stability of coumatetralyl Bayer CropScience AG, Report No.: MO-04-000677, Edition Number: MO-04-000677 Date: 2004-01-15 Non GLP, unpublished	Yes	BCS
6.1.1. /01	Bomann, W.	1992	Racumin techn. (c n. Coumatetralyl) - Investigations of acute oral toxicity in rats Bayer AG, Wuppertal, Germany Bayer CropScience AG, Report No.: 21726, Edition Number: MO-03-003991 Date: 1992-10-05 GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIA	Author(s)	Year	Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not	Data protect. claimed	Owner
6.1.1. /02	Bomann, W.	1992	Racumin techn. (c.n.: Coumatetralyl) - Investigations of acute oral toxicity in rabbits Bayer AG, Wuppertal, Germany Bayer CropScience AG, Report No.: 21727, Edition Number: MO-03-003999 Date: 1992-10-05 GLP, unpublished	Yes	BCS
6.1.2 /01	Bomann, W.	1992	Racumin techn. - Investigations of acute dermal toxicity in rats Bayer AG, Wuppertal, Germany Bayer CropScience AG, Report No.: 21729, Edition Number: MO-03-004039 Date: 1992-10-05 GLP, unpublished	Yes	BCS
4.2.1. /01	Brumhard, B.	2004	Method 00824 for the determination of residues of Coumatetralyl in soil by HPLC-MS/MS Bayer CropScience AG, Report No.: 00824, Edition Number: MO-04-000391 Method Report No.: MR-096/03 Date: 2004-01-13 GLP, unpublished	Yes	BCS
4.2.3. /01	Brumhard, B.	2004	Enforcement method 00820 for the determination of Coumatetralyl in drinking and surface water by HPLC-MS/MS Bayer CropScience AG, Report No.: 00820, Edition Number: MO-04-000390 Method Report No.: MR-076/03 Date: 2004-01-08 GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIA	**Author(s)**	**Year**	**Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not**	**Data protect. claimed**	**Owner**
7.1.1.2.1. /01	Desmares-Koopmans, M. J. E.; Van de Waart, E. J.	2001	Ready biodegrability : closed bottle test with coumatetralyl Notox B. V., S-Hertogenbosch, Netherland Bayer CropScience AG, Report No.: Notox 311873, Edition Number: MO-03-003122 Date: 2001-03-29 GLP, unpublished	Yes	BCS
7.1.1.2.2. /01	Desmares-Koopmans, M. J. E.; Van de waart, E. J.	2001	Inherent biodegradability : Zahn-Wellness/EMPA Test with coumatetralyl Notox, B. V., S-Hertogenbosch, Netherland Bayer CropScience AG, Report No.: Notox311884, Edition Number: MO-03-003141 Date: 2001-05-08 GLP, unpublished	Yes	BCS
7.5.1.2. /01	Erp, Y. H. M.	2001	Acute toxicity study in the earthworm eidenia fetida fetida with coumatetralyl Notox, B. V.; S-Hertogenbosch, Netherlands Bayer CropScience AG, Report No.: 311862, Edition Number: MO-03-002260 Date: 2001-12-31 GLP, unpublished also filed: Appendix 2. /10	Yes	BCS
3.9. /01	Erstling, K.; Jungheim, R.	2002	Partition coefficient (n-octanol/water) Racumin S technical (Coumatetralyl) Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: N 00/0106/07 LEV, Edition Number: MO-04-000231 Date: 2002-12-06 GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIA	Author(s)	Year	Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not	Data protect. claimed	Owner
3.5. /01	Erstling; Jungheim	2002	Racumin S technical (coumatetralyl) - Water solubility Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: N 00/0106/06 LEV, Edition Number: MO-04-000686 Date: 2002-11-28 GLP, unpublished	Yes	BCS
4.1. /04	Gerlach, ; Pohl,	1994	Racumin techn and Racumin S techn. ; Oxarin - High performance liquid chromatographic method ZF-DZA Analytic Uerdingen, Krefeld, Germany Bayer CropScience AG, Report No.: 2301-0222901-92, Edition Number: MO-04-000832 Date: 1994-04-19 Non GLP, unpublished	Yes	BCS
7.4.2. /01	Grau, R.	1992	Coumatetralyl bioconcentration in fish Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: BF-008, Edition Number: MO-03-003252 Date: 1992-05-07 GLP, unpublished also filed: Appendix 1. /09	Yes	BCS
7.4.3.1. /01	Grau, R.	1992	Coumateralyl (technical grade) prolonged toxicity (21 days) to rainbow trout in a semi-statistic test Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: FF-318, Edition Number: MO-03-003331 Date: 1992-06-05 GLP, unpublished also filed: Appendix 2. /05	Yes	BCS

Annex point/ reference number Doc IIIA	**Author(s)**	**Year**	**Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not**	**Data protect. claimed**	**Owner**
7.5.3.1.1. /01	Grau, R.	1992	Coumatetralyl (technical grade) acute oral toxicity to japanese quail Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: VW-158, Edition Number: MO-03-003614 Date: 1992-07-08 GLP, unpublished	Yes	BCS
7.5.3.1.2. /01	Grau, R.	1992	Coumatetralyl (technical grade) 5- day-dietary LC50 to japanese quail Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: VW-159, Edition Number: MO-03-003617 Date: 1992-06-30 GLP, unpublished also filed: Appendix 1. /08	Yes	BCS
7.4.1.2. /01	Heimbach, F.	1991	Acute toxicity of coumatetralyl (tech.) to waterfleas (daphnia magna) Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: HBF/Dm 107, Edition Number: MO-03-003177 Date: 1991-12-12 GLP, unpublished also filed: Appendix 2. /06	Yes	BCS
7.4.1.3. /01	Heimbach, F.	1991	Growth inhibition of green algae (Scenedesmus subspicatus) by coumatetralyl (tech.) Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: HBF/AL 96, Edition Number: MO-03-003167 Date: 1991-12-09 GLP, unpublished also filed: Appendix 2. /08	Yes	BCS

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7.4.3.4. /01	Heimbach, F.	1992	Influence of coumatetralyl (tech.) on the reproduction rate of water fleas Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: HBF/rDm 40, Edition Number: MO-03-003228 Date: 1992-01-13 GLP, unpublished also filed: Appendix 2. /07	Yes	BCS
3.11. /01	Heitkamp, D.	2001	Determination of safety-relevant data of Racumin S technical, coumatetralyl Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 00/00625, Edition Number: MO-03-003589 Date: 2001-01-22 GLP, unpublished also filed: 3.12. /01 also filed: 3.15. /01 also filed: 3.16. /01	Yes	BCS
3.12. /01	Heitkamp, D.	2001	Determination of safety-relevant data of Racumin S technical, coumatetralyl Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 00/00625, Edition Number: MO-03-003589 Date: 2001-01-22 GLP, unpublished also filed: 3.11. /01 also filed: 3.15. /01 also filed: 3.16. /01	Yes	BCS

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3.15. /01	Heitkamp, D.	2001	Determination of safety-relevant data of Racumin S technical, coumatetralyl Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 00/00625, Edition Number: MO-03-003589 Date: 2001-01-22 GLP, unpublished also filed: 3.11. /01 also filed: 3.12. /01 also filed: 3.16. /01	Yes	BCS
3.16. /01	Heitkamp, D.	2001	Determination of safety-relevant data of Racumin S technical, coumatetralyl Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 00/00625, Edition Number: MO-03-003589 Date: 2001-01-22 GLP, unpublished also filed: 3.11. /01 also filed: 3.12. /01 also filed: 3.15. /01	Yes	BCS
4.2.2. /01	Hellpointner, E.	2003	Enforcement method no. 00810 for the determination of coumatetralyl in air by HPLC-UV and confirmation via DAD-spectra matching Bayer CropScience AG, Report No.: 00810, Edition Number: MO-03-011359 Method Report No.: MEF-102/03 Date: 2003-07-25 GLP, unpublished	Yes	BCS
7.3.1.	Hellpointner, E	2003	E. Hellpointner. Calculation of the chemical lifetime of Coumatetralyl in the troposphere. Bayer CropScience AG , Development Metabolism / Environmental Fate,Monheim, Germany, BCS Report MEF-04/233, 2004-05-26	Yes	BCS

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6.6.1. /01	Herbold, B.	1986	ENE 11183B (c.n. coumatetralyl) - Salmonella/microsome test to evaluate for point mutagenic effect Bayer AG, Wuppertal, Germany Bayer CropScience AG, Report No.: 15070, Edition Number: MO-03-004013 Date: 1986-09-15 Non GLP, unpublished	Yes	BCS
6.6.1. /02	Herbold, B.	1986	ENE 11183B (c.n. coumatetralyl) - Test on S. cerevisiae D7 for the induction of mitotic recombination Bayer AG, Wuppertal, Germany Bayer CropScience AG, Report No.: 15071, Edition Number: MO-03-004056 Date: 1986-09-15 Non GLP, unpublished	Yes	BCS
6.6.3. /01	Herbold, B.	2004	Coumatetralyl - V79/HPRT-test in vitro for the detection of induced forward mutations Bayer HealthCare AG, Wuppertal, Germany Bayer CropScience AG, Report No.: AT00995, Edition Number: MO-04-001644 Date: 2004-02-13 GLP, unpublished	Yes	BCS
6.6.4. /01	Herbold, B.	1987	ENE 11183B (c.n. coumatetralyl) - Micronucleus test on the mouse to evaluate for clastogenic effect Bayer AG, Wuppertal, Germany Bayer CropScience AG, Report No.: 15407, Edition Number: MO-03-004060 Date: 1987-01-12 GLP, unpublished	Yes	BCS

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3.1.1 /01	Jungheim	2000	Racumin S technical, coumatetralyl - physical und chemical properties Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: N 00/0106/01 LEV, Edition Number: MO-03-003568 Date: 2000-11-08 GLP, unpublished also filed: 3.1.2 /01 also filed: 3.1.3 /01 also filed: 3.10. /01	Yes	BCS
3.1.2 /01	Jungheim	2000	Racumin S technical, coumatetralyl - physical und chemical properties Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: N 00/0106/01 LEV, Edition Number: MO-03-003568 Date: 2000-11-08 GLP, unpublished also filed: 3.1.1 /01 also filed: 3.1.3 /01 also filed: 3.10. /01	Yes	BCS
3.1.3 /01	Jungheim	2000	Racumin S technical, coumatetralyl - physical und chemical properties Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: N 00/0106/01 LEV, Edition Number: MO-03-003568 Date: 2000-11-08 GLP, unpublished also filed: 3.1.1 /01 also filed: 3.1.2 /01 also filed: 3.10. /01	Yes	BCS

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3.6. /01	Jungheim	2001	Racumin S technical, coumatetralyl - Dissociation constant/solubility in organic solvents Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: N 00/0106/04 LEV, Edition Number: MO-03-003583 Date: 2001-02-05 GLP, unpublished also filed: 3.7. /01	Yes	BCS
3.7. /01	Jungheim	2001	Racumin S technical, coumatetralyl - Dissociation constant/solubility in organic solvents Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: N 00/0106/04 LEV, Edition Number: MO-03-003583 Date: 2001-02-05 GLP, unpublished also filed: 3.6. /01	Yes	BCS
3.10. /01	Jungheim	2000	Racumin S technical, coumatetralyl - physical und chemical properties Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: N 00/0106/01 LEV, Edition Number: MO-03-003568 Date: 2000-11-08 GLP, unpublished also filed: 3.1.1 /01 also filed: 3.1.2 /01 also filed: 3.1.3 /01	Yes	BCS
3.4.1 /01	Kaussmann, M.	2000	Spectral data set of coumatertralyl Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 15-600-2136, Edition Number: MO-03-003578 Date: 2000-12-13 GLP, unpublished also filed: 3.4.2 /01 also filed: 3.4.3 /01 also filed: 3.4.4 /01	Yes	BCS

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3.4.2 /01	Kaussmann, M.	2000	Spectral data set of coumatertralyl Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 15-600-2136, Edition Number: MO-03-003578 Date: 2000-12-13 GLP, unpublished also filed: 3.4.1 /01 also filed: 3.4.3 /01 also filed: 3.4.4 /01	Yes	BCS
3.4.3 /01	Kaussmann, M.	2000	Spectral data set of coumatertralyl Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 15-600-2136, Edition Number: MO-03-003578 Date: 2000-12-13 GLP, unpublished also filed: 3.4.1 /01 also filed: 3.4.2 /01 also filed: 3.4.4 /01	Yes	BCS
3.4.4 /01	Kaussmann, M.	2000	Spectral data set of coumatertralyl Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 15-600-2136, Edition Number: MO-03-003578 Date: 2000-12-13 GLP, unpublished also filed: 3.4.1 /01 also filed: 3.4.2 /01 also filed: 3.4.3 /01	Yes	BCS

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6.1.3. /01	Lautraite, S.	2003	Coumatetralyl - Waiver for acute and sub-chronic toxicity studies in rat by inhalation Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: MO-03-015576, Edition Number: MO-03-015576 Date: 2003-12-08 Non GLP, unpublished also filed: 6.1.3. /01 also filed: 6.4.3. /01	Yes	BCS
6.4.1.2. /01	Lautraite, S.	2003	Coumatetralyl - Waiver for chronic toxicity study in dogs, chronic/carcinogenicity toxicity study in rodents, and multigeneration study in rodents Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: MO-03-006927, Edition Number: MO-03-006927 Date: 2003-05-22, Amended: 2003-06-05 Non GLP, unpublished also filed: 6.5. /01 also filed: 6.7. /01 also filed: 6.8.2. /01 also filed: 6.9. /01	Yes	BCS
6.4.3. /01	Lautraite, S.	2003	Coumatetralyl - Waiver for acute and sub-chronic toxicity studies in rat by inhalation Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: MO-03-015576, Edition Number: MO-03-015576 Date: 2003-12-08 Non GLP, unpublished also filed: 6.1.3. /01	Yes	BCS

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6.5. /01	Lautraite, S.	2003	Coumatetralyl - Waiver for chronic toxicity study in dogs, chronic/carcinogenicity toxicity study in rodents, and multigeneration study in rodents Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: MO-03-006927, Edition Number: MO-03-006927 Date: 2003-05-22, Amended: 2003-06-05 Non GLP, unpublished also filed: 6.4.1.2. /01 also filed: 6.7. /01 also filed: 6.8.2. /01 also filed: 6.9. /01	Yes	BCS
6.7. /01	Lautraite, S.	2003	Coumatetralyl - Waiver for chronic toxicity study in dogs, chronic/carcinogenicity toxicity study in rodents, and multigeneration study in rodents Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: MO-03-006927, Edition Number: MO-03-006927 Date: 2003-05-22, Amended: 2003-06-05 Non GLP, unpublished also filed: 6.4.1.2. /01 also filed: 6.5. /01 also filed: 6.8.2. /01 also filed: 6.9. /01	Yes	BCS
6.8.2. /01	Lautraite, S.	2003	Coumatetralyl - Waiver for chronic toxicity study in dogs, chronic/carcinogenicity toxicity study in rodents, and multigeneration study in rodents Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: MO-03-006927, Edition Number: MO-03-006927 Date: 2003-05-22, Amended: 2003-06-05 Non GLP, unpublished also filed: 6.4.1.2. /01 also filed: 6.5. /01 also filed: 6.7. /01 also filed: 6.9. /01	Yes	BCS

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6.9. /01	Lautraite, S.	2003	Coumatetralyl - Waiver for chronic toxicity study in dogs, chronic/carcinogenicity toxicity study in rodents, and multigeneration study in rodents Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: MO-03-006927, Edition Number: MO-03-006927 Date: 2003-05-22, Amended: 2003-06-05 Non GLP, unpublished also filed: 6.4.1.2. /01 also filed: 6.5. /01 also filed: 6.7. /01 also filed: 6.8.2. /01	Yes	BCS
2.10. /01	Maasfeld, W.; Mueller, G.	2004	Determination of operator exposure to Coumatetralyl during application and disposal of Racumin paste by professionals and amateurs Bayer CropScience AG, Report No.: MR-203/03, Edition Number: MO-04-000557 Date: 2004-01-16 GLP, unpublished also filed: Appendix 3. /02	Yes	BCS
7.4.1.4. /01	Mueller, G.; Hartmann, P.	1991	Study of ecological behaviour of Racumin S Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 283 A/91, Edition Number: MO-03-003165 Date: 1991-07-12 GLP, unpublished	Yes	BCS
4.2.4. /02	Mundy, D. E.; Machin, A. F.	1982	The multi-resiude determination of coumarin-based anticoagulant Rodenticides in animal materials by high-performance liquid chromatography Ministry of Agriculture Fisheries and Food, Surrey, Great Britain Bayer CropScience AG, Report No.: 00075, Edition Number: MO-03-003654 Method Report No.: I393 Date: 1982-01-01 Non GLP, published	No	

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4.1. /07	Nonn, E.	1990	Digestion solutions and aqueous phases; Chloride, Phosphate, Nitrate and Sulfate Bayer AG, Dormagen, Germany Bayer CropScience AG, Report No.: 2201-0217701-90, Edition Number: MO-99-011757 Date: 1990-10-30 Non GLP, unpublished	Yes	BCS
4.1. /03	Odendahl, A.	2002	Validation of HPLC-method 2001-0004804-02 - Determination of Coumatetralyl in formulations- Bayer CropScience AG, Report No.: VB1-2001-0004804, Edition Number: MO-02-014014 Date: 2002-09-10 Non GLP, unpublished also filed: 4.1. /02	Yes	BCS
3.2. /01	Olf	2000	Racumin S technical, coumatetralyl - Vapor pressure, physical-chemical properties Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 00/028/01, Edition Number: MO-03-003573 Date: 2000-10-20 GLP, unpublished	Yes	BCS
3.13. /01	Olf	2001	Racumin S technical, coumatetralyl - surface tension, physical-chemical properties Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 00/28/03, Edition Number: MO-03-003639 Date: 2001-01-17 GLP, unpublished	Yes	BCS
6.6.2. /01	Renault, D.	2004	Coumatetralyl - Waiver for genotoxicity studies Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: MO-04-001741, Edition Number: MO-04-001741 Date: 2004-02-15 Non GLP, unpublished	Yes	BCS

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6.1.4. /01	Renhof, M.	2003	Coumatetralyl - Acute eye irritation/corrosion on rabbits Bayer HealthCare AG, Wuppertal, Germany Bayer CropScience AG, Report No.: AT00880, Edition Number: MO-03-015921 Date: 2003-12-17 GLP, unpublished	Yes	BCS
6.1.4. /02	Renhof, M.	2003	Coumatetralyl - Acute skin irritation/corrosion on rabbits Bayer HealthCare AG, Wuppertal, Germany Bayer CropScience AG, Report No.: AT00739, Edition Number: MO-03-013919 Date: 2003-10-27 GLP, unpublished	Yes	BCS
4.1. /02	Seidel, E.	2002	Determination of Coumatetralyl in formulations ; Assay - HPLC - external standard Bayer CropScience AG, Report No.: 2001-0004804-02, Edition Number: MO-02-014117 Date: 2002-09-23 Non GLP, unpublished also filed: 4.1. /01	Yes	BCS
7.4.1.1. /01	Sewell, J. G.; McKenzie, J.	2003	Coumatetralyl (technical) - Acute toxicity to rainbow trout (Oncorhynchus mykiss) Safepharm Laboratories Limited, Shardlow, Great Britain Bayer CropScience AG, Report No.: 1392/052, Edition Number: MO-04-001275 Date: 2003-12-04 GLP, unpublished also filed: Appendix 2. /09	Yes	BCS

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7.1.3. /01	Slangen, P. J.	2002	Development and validation report of an analytical method for coumatetralyl and soil adsorption/desorption of coumatetralyl on five soils (screening test) Notox, S-Hertogenbosch, Netherland Bayer CropScience AG, Report No.: 333473, Edition Number: MO-03-003147 Date: 2002-03-29 GLP, unpublished	Yes	BCS
2.7. /01	Stepec	1998	Product specification of Racumin S tech. Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: MO-03-003535, Edition Number: MO-03-003535 Date: 1998-11-02 Non GLP, unpublished	Yes	BCS
3.2.1 /01	Stoecker, R. H.	2004	Henry`s law constan of Racimin S technical (coumatetralyl) Bayer Environmental Science, Monheim, Germany Bayer CropScience AG, Report No.: SKD Hen 01/04, Edition Number: MO-04-000993 Date: 2004-01-27 GLP, unpublished	Yes	BCS
3.3. /01	Stoecker, R. H.; Rosenfeldt, F.	2003	Appearance of the substance racumin paste Bayer CropScience AG, Report No.: SKD APP 07/03, Edition Number: MO-04-000247 Date: 2003-08-31 Non GLP, unpublished also filed: 3.1. /01	Yes	BCS
6.1.5. /01	Stropp, G.	1998	Racumin techn. S - Study for the skin sensitization effect in guinea pigs (Buehler Patch Test) Bayer AG, Wuppertal, Germany Bayer CropScience AG, Report No.: 27301, Edition Number: MO-03-002277 Date: 1998-03-17 GLP, unpublished	Yes	BCS

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2.8. /01	Veith; Haustein	2000	GLP - Final report, material accountability study Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: MO-03-003185, Edition Number: MO-03-003185 Date: 2000-12-01 GLP, unpublished	Yes	BCS
7.1.1.1.1. /01	Wilmes, R.	1983	Fate/ Behaviour of crop protection products in water Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: MO-03-002794, Edition Number: MO-03-002794 Date: 1983-03-23 Non GLP, unpublished	Yes	BCS
7.1.1.1.2. /01	Wilmes, R.	1982	Orientating light stability Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: MO-03-003648, Edition Number: MO-03-003648 Date: 1982-05-21 Non GLP, unpublished also filed: Appendix 2. /11	Yes	BCS
4.2.4. /01	Wright, G.; Radford, C.; Fisher, P.	2003	Determination of Coumatetralyl in liver by HPLC : Methodology and validation of analyses Landcare Research New Zealand, New Zealand Bayer CropScience AG, Report No.: MO-04-001349, Edition Number: MO-04-001349 Date: 2003-12-31 Non GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIB	**Author(s)**	**Year**	**Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not**	**Data protect. claimed**	**Owner**
IX. /01	Anon.	2003	Racumin paste Bayer CropScience AG, Report No.: 875113/04, Edition Number: MO-04-002718 Date: 2003-09-01 Non GLP, unpublished also filed: I.1.3. /01	Yes	BCS
3.3. /01	Boecker, T.	2004	Statement on the oxidizing properties of the Racumin paste Bayer CropScience AG, Report No.: MO-04-001403, Edition Number: MO-04-001403 Date: 2004-01-27 Non GLP, unpublished	Yes	BCS
3.7. /01	Doth, M.; Stoecker, R. H.	2003	Product: Racumin RB paste - Compilation of product stability data and shelf life assessment - Interim report at 36 months of storage Bayer CropScience AG, Report No.: SKD STAB 102/03, Edition Number: MO-04-000694 Date: 2003-10-17 Non GLP, unpublished	Yes	BCS
5.10.2. /02	Endepols, S.	1998	Efficacy of Racumin paste administered for one day in a no-choice trail with wild rats (Rattus norvegicus) Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: END04998, Edition Number: MO-03-003559 Date: 1998-05-20 Non GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIB	Author(s)	Year	Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not	Data protect. claimed	Owner
5.10.2. /04	Endepols, S.	1997	Biological efficacy of Racumin paste (0.04 percent coumatetralyl) stored at 50 degreed C for 2,4, and 8 weeks on wild Norway rats (Rattus norvegicus) Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: END14196, Edition Number: MO-03-004057 Date: 1997-02-12 Non GLP, unpublished	Yes	BCS
5.10.2. /05	Endepols, S.	1998	Biological efficacy of Racumin paste (0.0375 percent coumatetralyl) stored up to one year-synopsis of 12 laboratory trials with wild Norway rats (Rattus norvegicus) Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: END09797, Edition Number: MO-03-003728 Date: 1998-05-12 Non GLP, unpublished	Yes	BCS
5.10.2. /06	Endepols, S.	1996	Field trail with Racumin paste containing 400 ppm Coumatetralyl against rats at a farm in the Muensterland area, Germany Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: END16896, Edition Number: MO-03-003584 Date: 1996-12-18 Non GLP, unpublished	Yes	BCS
5.10.2. /07	Endepols, S.	1996	Field trail with Racumin Paste containing 375 ppm coumatetralyl, packed in collagen skin against Norway rats (Rattus norvegicus) at a chicken farm in Leverkusen, Germany Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: END10096, Edition Number: MO-03-004061 Date: 1996-09-03 Non GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIB	**Author(s)**	**Year**	**Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not**	**Data protect. claimed**	**Owner**
5.10.2. /08	Endepols, S.	1997	Field trail with Racumin Paste containing 375 ppm coumatetralyl, packed in cellulose skin against Norway rats (Rattus norvegicus) in a Warehouse in Monheim, Germany Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: END05596, Edition Number: MO-03-004063 Date: 1997-01-14 Non GLP, unpublished	Yes	BCS
5.10.2. /09	Endepols, S.	1997	Efficacy of Racumin paste with 0.04 percent Coumatetralyl for the control of rats (Rattus Norvegicus) at a composting plant Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: END16796, Edition Number: MO-03-003587 Date: 1997-01-16 Non GLP, unpublished	Yes	BCS
5.10.2. /03	Grolleau, G.	1996	Acceptance and efficacy of a bait containing 0.04 percent coumatetralyl administered to Norway rats (Rattus norvegicus) INRA-Phytopharmaceutical and Chemical Mediators Unit, Versailles, France Bayer CropScience AG, Report No.: MO-03-003570, Edition Number: MO-03-003570 Date: 1996-10-25 Non GLP, unpublished	Yes	BCS
3.2. /01	Heinz, U.	2002	Determination of safety-relevant data of Racumin Paste Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 02/00229, Edition Number: MO-04-000237 Date: 2002-05-29 GLP, unpublished also filed: 3.4. /01	Yes	BCS

Annex point/ reference number Doc IIIB	Author(s)	Year	Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not	Data protect. claimed	Owner
3.4. /01	Heinz, U.	2002	Determination of safety-relevant data of Racumin Paste Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 02/00229, Edition Number: MO-04-000237 Date: 2002-05-29 GLP, unpublished also filed: 3.2. /01	Yes	BCS
3.8. /01	Heinz, U.	2002	Determination of safety-relevant data of Racumin Paste Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 02/00344, Edition Number: MO-04-000238 Date: 2002-06-29 GLP, unpublished also filed: 3.10.2. /01	Yes	BCS
3.10.2. /01	Heinz, U.	2002	Determination of safety-relevant data of Racumin Paste Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 02/00344, Edition Number: MO-04-000238 Date: 2002-06-29 GLP, unpublished also filed: 3.8. /01	Yes	BCS
5.10.2. /11	Iglisch, I.	1997	Testing of "Racumin Paste" for efficacy against brown rats in the biotope in accordance with paragraph 10 c of the Bundes-Seuchengesetz (contagious diseases law) Umweltbundesamt, Berlin, Germany Bayer CropScience AG, Report No.: V1.8-8460-C20/97, Edition Number: MO-03-004082 Date: 1997-07-15 Non GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIB	Author(s)	Year	Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not	Data protect. claimed	Owner
3.5. /01	Jungheim, R.	2002	GLP final report : Physicochemical properties of the Racumin paste Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: MO-03-003752, Edition Number: MO-03-003752 Date: 2002-06-28 GLP, unpublished also filed: 3.6. /01	Yes	BCS
3.6. /01	Jungheim, R.	2002	GLP final report : Physicochemical properties of the Racumin paste Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: MO-03-003752, Edition Number: MO-03-003752 Date: 2002-06-28 GLP, unpublished also filed: 3.5. /01	Yes	BCS
6.1.3. /01	Lautraite, S.	2003	Coumatetralyl - Waiver for acute and sub-chronic toxicity studies in rat by inhalation Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: MO-03-015576, Edition Number: MO-03-015576 Date: 2003-12-08 Non GLP, unpublished also filed: 6.1.3. /01 also filed: 6.4.3. /01	Yes	BCS
6.2. /01	Leuschner, J.	1997	Acute eye irritation study of Racumin paste (0,0375%) by instillation into the conjunctival sac of rabbits LPT, Laboratory of Pharmacology and Toxicology, Hamburg, Germany Bayer CropScience AG, Report No.: R7014, Edition Number: MO-03-002263 Date: 1997-12-22 GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIB	**Author(s)**	**Year**	**Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not**	**Data protect. claimed**	**Owner**
6.2. /02	Leuschner, J.	1997	Acute skin irritation test (patch test) of Racumin paste (0,0375%) in rabbits LPT, Laboratory of Pharmacology and Toxicology, Hamburg, Germany Bayer CropScience AG, Report No.: R7013, Edition Number: MO-03-002261 Date: 1997-12-11 GLP, unpublished	Yes	BCS
4.1. /02	Odendahl, A.	2002	Validation of HPLC-method 2001-0004804-02 -Determination of Coumatetralyl in formulations- Bayer CropScience AG, Report No.: VB1-2001-0004804, Edition Number: MO-02-014014 Date: 2002-09-10 Non GLP, unpublished also filed: 4.1. /03	Yes	BCS
6.4. /01	Odin-Feurtet, M.	2003	[14C]-Coumatetralyl - Comparative in vitro dermal absorption study using human and rat skin Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: SA 03109, Edition Number: MO-03-014033 Date: 2003-10-03, Amended: 2003-10-22 GLP, unpublished	Yes	BCS
6.4. /02	Odin-Feurtet, M.	2003	[14C]-Coumatetralyl - In vivo dermal absorption study in the male rat Bayer CropScience, Sophia Antipolis, France Bayer CropScience AG, Report No.: SA 03108, Edition Number: MO-03-013323 Date: 2003-10-02 GLP, unpublished	Yes	BCS

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3.10.1. /01	Olf, G.	2003	Surface tension, physical-chemical properties - Racumin paste Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: 02/014/03, Edition Number: MO-04-000241 Date: 2003-02-19 GLP, unpublished	Yes	BCS
5.10.2. /01	Pospischil, R.	1998	Racumin Paste - Coumatetrallyl 0.0375 percent - Efficacy Bayer AG, Leverkusen, Germany Bayer CropScience AG, Report No.: MO-03-003554, Edition Number: MO-03-003554 Date: 1998-09-11 Non GLP, unpublished	Yes	BCS
5.10.2. /12	Rashid, M. Z. A.	1997	Racumin paste field trail - 0,037 percent coumatetralyl Bayer Sdn. Bhd., Shah Alam, Malaysia Bayer CropScience AG, Report No.: MZ001/97, Edition Number: MO-03-003721 Date: 1997-11-01 Non GLP, unpublished	Yes	BCS
6.1.1. /01	Schuengel, M.	2003	Coumatetralyl 0.0375% paste bait - Acute toxicity in the rat after oral administration Bayer HealthCare, Wuppertal, Germany Bayer CropScience AG, Report No.: AT00730, Edition Number: MO-03-013836 Date: 2003-10-24 GLP, unpublished	Yes	BCS
6.1.2 /01	Schuengel, M.	2003	Coumatetralyl 0.0375% paste bait - Acute toxicity in the rat after dermal administration Bayer HealthCare, Wuppertal, Germany Bayer CropScience AG, Report No.: AT00729, Edition Number: MO-03-013838 Date: 2003-10-24 GLP, unpublished	Yes	BCS

Annex point/ reference number Doc IIIB	**Author(s)**	**Year**	**Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not**	**Data protect. claimed**	**Owner**
5.10.2. /10	Schuster, W.	1997	Acceptance and efficacy of Racumin paste (0.04 percent coumatetralyl) against brown rats (Rattus norvegicus) in the sewage system Hygieneinstitut Magdeburg, Magdeburg, Germany Bayer CropScience AG, Report No.: WR-Biot.97, Edition Number: MO-03-003590 Date: 1997-05-23 Non GLP, unpublished	Yes	BCS
4.1. /01	Seidel, E.	2002	Determination of Coumatetralyl in formulations ; Assay - HPLC - external standard Bayer CropScience AG, Report No.: 2001-0004804-02, Edition Number: MO-02-014117 Date: 2002-09-23 Non GLP, unpublished also filed: 4.1. /02	Yes	BCS
3.7. /02	Stoecker, R. H.	2004	Product: Racumin Paste - Shelf life evaluation under real time conditions - Quality assurance status of laboratories involved Bayer CropScience AG, Report No.: MO-04-000682, Edition Number: MO-04-000682 Date: 2004-01-12 Non GLP, unpublished	Yes	BCS
3.1. /01	Stoecker, R. H.; Rosenfeldt, F.	2003	Appearance of the substance racumin paste Bayer CropScience AG, Report No.: SKD APP 07/03, Edition Number: MO-04-000247 Date: 2003-08-31 Non GLP, unpublished also filed: 3.3. /01	Yes	BCS

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6.3. /01	Vohr, H.-W.	2004	Coumatetralyl 0.0375% paste bait - Study for the skin sensitization effect in guinea pigs (guinea pig maximization test according to Magnusson and Kligman) Bayer HealthCare AG, Wuppertal, Germany Bayer CropScience AG, Report No.: AT00925, Edition Number: MO-04-000702 Date: 2004-01-26 GLP, unpublished	Yes	BCS