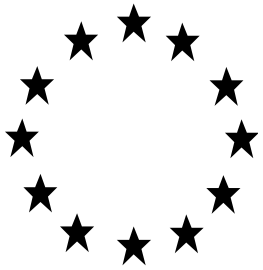
Directive 98/8/EC concerning the placing of biocidal products on the market

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

Assessment Report



Difenacoum

Product-type 14 (Rodenticides)

17 September 2009

Annex I - Finland

Difenacoum (PT 14)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 29 November 2007 in view of its inclusion in Annex I to Directive 98/8/EC

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1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

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

Difencoum (CAS no. 56073-07-5) was notified as an existing active substance, by Sorex Limited, Hentschke & Sawatzki KG, and the Activa/Pelgar Difenacoum and Brodifacoum Task Force, hereafter referred to as the applicants 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, Finland was designated as Rapporteur Member State to carry out the assessment on the basis of the dossiers submitted by the applicants. The deadline for submission of a complete dossier for difenacoum as an active substance in product-type 14 was 28 March 2004, in accordance with Annex V of Regulation (EC) No 2032/2003.

On 24 and 26 March 2004, the Finnish competent authorities received the dossiers from all of the applicants. The Rapporteur Member State accepted the dossiers as complete for the purpose of the evaluation on 24 September 2004. The dossier of Activa/Pelgar Difenacoum and Brodifacoum Task Force was not complete and the applicant agreed to submit further data in order to complete the dossier. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 6 February 2006.

On 21 March 2006, the Rapporteur Member State submitted, in accordance with the provisions of Article 10(5) and (7) of Regulation (EC) No 2032/2003, to the Commission and the applicants a copy of the evaluation reports, hereafter referred to as the competent authority reports. The competent authority report of the Activa/Pelgar Difenacoum and Brodifacoum Task Force was submitted on 6 February 2008. The Commission made the reports available to all Member States by electronic means on 12 April 2006. The report of Activa/Pelgar Difenacoum and Brodifacoum Task Force was made available to all Member States by

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

electronic means on 15 February 2008. The competent authority reports included a recommendation for the inclusion of difenacoum in Annex I to the Directive for PT 14.

In accordance with Article 12 of Regulation (EC) No 2032/2003, the Commission made the competent authority reports publicly available by electronic means on 24 April 2006 and on 18 February 2008. These reports 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 reports 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 reports were amended accordingly. The merged conclusions of the risk assessment are presented in this assessment report.

On the basis of the final competent authority reports, the Commission proposed the inclusion of difenacoum in Annex I to Directive 98/8/EC and consulted the Standing Committee on Biocidal Product on 29 November 2007.

In accordance with Article 11(4) of Regulation (EC) No 2032/2003, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 29 November 2007.

The addition of the Activa/PelGar Brodifacoum and Difenacoum Task Force data to the Difenacoum Assessment Report was agreed upon at the 34th Competent Authority Meeting on 17 September 2009.

1.2. Purpose of the assessment report

This assessment report has been developed and finalised in support of the decision to include difenacoum 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 difenacoum. In their evaluation, Member States shall apply the provisions of Directive 98/8/EC, in particular the provisions of Article 5 as well as the common principles laid down in Annex VI.

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

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

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

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 difenacoum for the product-type 14, which will fulfil many of the requirements laid down in Article 10(1) and (2) of Directive 98/8/EC but not in all cases, such as in accidental incidents to children and when posing unacceptable environmental risk to non-target animals. However, difenacoum is for the time being considered essential for reasons of public health and hygiene which justifies inclusion of difenacoum in Annex I. This conclusion is moreover subject to:

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

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

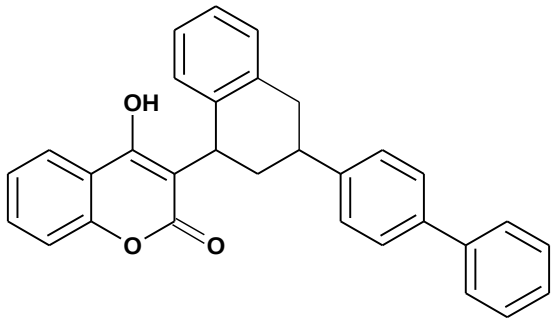
iii. the common principles laid down in Annex VI to Directive 98/8/EC.

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

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

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

CAS-No.	56073-07-5
EINECS-No.	259-978-4
Other No. (CIPAC, ELINCS)	67/548/EEC Annex I N$^{o.}$: 607-157-00-X
IUPAC Name	3-(3-biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphthyl)-4-hydroxycoumarin
CAS Name	2H-1-Benzo pyran-2-one, 3-(3-[1,1'-biphenyl]-4-yl-1,2,3,4-tetrahydro-1-naphthalenyl)-4-hydroxy-
Common name, synonyms	Difenacoum (BSI, ISO), diphenacoum
Molecular formula	$C_{31}H_{24}O_3$
Structural formula	
Molecular weight (g/mol)	444.5
Purity	≥ 960 g/kg
Isomers	Isomeric mixture of trans isomer (CAS N. 151986-16-2, CA Index Name: 2H-1-Benzopyran-2-one, 3-(3-[1,1'-biphenyl]-4-yl-1,2,3,4-tetrahydro-1-naphthalenyl)-4-hydroxy-, trans-) and cis isomer (CAS N. 151986-15-1, CA Index Name: 2H-1-Benzopyran-2-one, 3-(3-[1,1'-biphenyl]-4-yl-1,2,3,4-tetrahydro-1-naphthalenyl)-4-hydroxy-, cis-). The range of cis-isomer is 50-80%. Both diastereomers are toxicologically active. More detailed information on isomers is given in Annex Confidential Data and Information. Note that each applicant has a separate confidential annex.

Difenacoum does not contain additives or impurities that would be of toxicological or environmental concern. The full details of identity of the active substance are confidential and can be found in the Annex Confidential Data and Information. The minimum purity of 960 g/kg is supported by the analytical data (5-batch analysis) and it has been used in most of the toxicity and ecotoxicity tests in dossiers of Sorex Limited and Hentschke & Sawatzki KG. A higher minimum purity, 995 g/kg, is supported by the analytical data and it has been used in most of the toxicity and ecotoxicity studies in the dossier of the Activa/PelGar. From the two diastereomeric pairs of enantiomers, the (1*RS*, 3*SR*) pair (*cis*) is more slowly metabolised and acutely slightly more toxic than the (1*RS*, 3*RS*) pair (*trans*) based on dossier provided by Sorex Limited but there is no further studies. Both specifications have been accepted and, thus, the minimum purity of 960 g/kg shall apply for difenacoum. For other specifications and isomeric contents at least bridging studies are needed.

Difenacoum does not exhibit hazardous physical-chemical properties. Difenacoum is a white to off-white powder (off-white to beige, technical grade). It has low vapour pressure; Henry's law constant (1.75×10^{-6} Pa m^3 mol^{-1} or <0.046 Pa m^3 mol^{-1}) was calculated based on an estimated value of 6.7×10^{-9} Pa at 25 ^oC or on an estimated vapour pressure of less than 5×10^{-5} Pa at 45 °C). Difenacoum is a weak acid with a pKa value of 4.84 or with an estimated pKa value of 4.5 + 1. The water solubility is pH dependent and it increases with increasing pH. At neutral conditions the water solubility of difenacoum is low, 1.7 mg/l (at pH 7 at 20 ^oC), or in 0.48 mg/l (at 20 °C at pH 6.5). Solubilitiy in organic solvents tested ranged from 1 to 20 g/l. The estimated log K_{ow} value is 7.6. The experimental information available on difenacoum suggests that it may be beyond the performance ranges of the experimental tests for log K_{ow}. The substance is thermally stable up to about 300 ^oC or up to 250 ^oC. No boiling point was detected before start of decomposition. Difenacoum is not highly flammable, and it shows no self-ignition at temperatures up to melting point, 211-215 ^oC or 215 ^oC, the maximum temperature in the test). Corrosiveness to containers has not been observed. Difenacoum does not show oxidizing or explosive properties. There is no risk to be expected due to the physical-chemical properties of the formulated product.

Acceptable methods for determination of difenacoum and associated impurities present at quantities >0.1% w/w in the technical grade material as manufactured are available. Sorex Limited has no acceptable method for analysis of difenacoum in formulation, but the participant is undertaking a new validation for such a method and this requirement should be fulfilled at the product authorisation stage. This data requirement is fulfilled by the two other participants.

Sorex Limited and Hentschke & Sawatzki KG have acceptably validated analytical methods of difenacoum in soil, water, sediment and liver. The methods are considered to be sufficiently sensitive with respect to the levels of concern. An acceptable analytical method for the determination of residues of difenacoum in/on food or feedingstuffs is available which enables the analysis down to level of 0.01 mg/kg. In all residue methods HPLC-MS/MS methodology is used, except in the method of analysis for liver which is performed with HPLC followed by fluorescence detection.

The Activa/PelGar Brodifacoum and Difenacoum Task Force has acceptably validated methods for the analysis of difenacoum in soil and water. The methods are regarded to be sufficiently sensitive with respect to the levels of concern. Validation data for analytical method in

sediment is required for the product authorisation. An acceptable analytical method for the determination of residues of difenacoum food matrices (cucumber, wheat and lemon) is available which enables the analysis down to level of 0.01 mg/kg, but no acceptable validation data for meat and oil-seed-rape is available. Validation data for these food matrices (meat and oil-seed-rape) and also a validated method for the analysis of difenacoum in animal and human tissues (liver) should be submitted at the product evaluation stage.

2.1.2. Intended Uses and Efficacy

Difenacoum is intended to be used to control rodent pests in and around buildings, in open areas, around waste sites and in sewers. The target species are brown rat (*Rattus norvegicus)*, black rat (*Rattus rattus)* and house mouse (*Mus musculus/domesticus)*. Summary of intended uses is given in Appendix II.

The assessment of the biocidal activity of difenacoum demonstrates that it has a sufficient level of efficacy against the target organisms in concentration of 50 mg/kg 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. Difenacoum content in the representative products ranges from 50 – 75 mg/kg.

Difenacoum is a second generation anticoagulant which prevents blood clotting in the target organisms by inhibiting regeneration of the active form of vitamin K_1. Clinical signs are progressive and occur within 18 hours after ingestion of a toxic dose, ultimately leading to death from 3 to 10 days later. Effects are reversible by administration of the antidote vitamin K_1 which stimulates the regeneration of the clotting factors.

The use of difenacoum as a rodenticide could cause suffering of vertebrate target organisms. The use of anticoagulant rodenticides is necessary as there are at present no other equally effective 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 Article 5.1 of Directive 98/8/EC ‘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 performed when possible alternatives have been evaluated and all data are available.

Difenacoum resistant brown rats are found in limited areas of Denmark, Germany and Great Britain. Monitoring of resistance occurs only in these countries and lack of information does not necessarily mean lack of resistance in the other countries. The incidence of resistance ranges from 2 to 84%. About 5-9-fold doses are needed to kill difenacoum resistant rats. No reports have been submitted to the Rapporteur Member State about the distribution and incidence of resistance in the house mouse or black rat in Europe.

2.1.3. Classification and Labelling

On the basis of review of the submitted data and read-across of data from warfarin, the Rapporteur Member State (RMS) suggests that the current classification of difenacoum (health hazard) in Annex I to Directive 67/548/EEC is revised. Specific concentration limits have been proposed for the environmental classification.

Classification	T+; R26/27/28, Repr. Cat. 1; R61, T; 48/23/24/25, N; R50/53	
Category of danger	Very Toxic, Dangerous for the Environment	
R phrases	R26/27/28, Very Toxic by inhalation, in contact with skin and if swallowed.	
	R48/23/24/25, Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.	
	R61, May cause harm to the unborn child.	
	R50/53, Very Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.	
S phrases	S45, In case of accident or if you feel unwell, seek medical advice immediately (show label where possible).	
	S53, Avoid exposure - obtain special instruction before use.	
	S60, This material and/or its container must be disposed of as hazardous waste.	
	S61 Avoid release to the environment. Refer to special instructions/safety data sheet.	
Specific concentration limits for the human and environmental classification	$C \geq 2.5\%$	T+, N; R26/27/28-48/23/24/25-61-50-53
	$0.5\% \leq C < 2.5\%$	T+, N; R26/27/28-48/23/24/25-61-51-53
	$0.25\% \leq C < 0.5\%$	T+, N; R26/27/28-48/23/24/25-51-53
	$0.025\% \leq C < 0.25\%$	T ; R23/24/25-48/20/21/22-52-53
	$0.0025\% \leq C < 0.025\%$	Xn; R20/21/22

No classification of products containing 50 mg/kg or 75 mg/kg difenacoum would be necessary according to Directive 1999/45/EC. However, specific concentration limits of difenacoum have been agreed by the Technical Committee on Classification and Labelling.

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Critical end points

Difenacoum is a so-called second generation anticoagulant, which causes death of target organisms due to massive internal haemorrhages after several days of ingestion of a lethal dose. Difenacoum is very toxic by inhalation, in contact with skin and if swallowed.

Difenacoum, like other coumarin derivatives, acts as a vitamin K antagonist through inhibition of vitamin K reductase leading to depletion of a number of carboxylated blood coagulation factors. The effect is cumulative in nature. Haemorrhaging and subsequent death is the only effect observed in acute and repeated-dose toxicity tests. Prolongation of prothrombin time is usually observed before clinical signs of toxicity.

Furthermore, as difenacoum contains the same chemical moiety responsible for the teratogenicity of warfarin, a known human teratogenic substance, and it has the same mode of action (inhibition of vitamin K hydroquinone regeneration) that is a known mechanism of teratogenicity in humans, it can also be considered teratogenic and developmentally toxic. The Specialised Experts unanimously agreed on read-across from warfarin at their meeting in September 2006, but the discussion at the Technical Committee on Classification and Labelling is not completed at the time of decision making in the Standing Committee on Biocidal Products.

2.2.1.2. Toxicokinetics

Absorption of difenacoum after oral intake of a single 0.1 mg/kg bw dose is 68% (bile, urine, liver and carcass included). Without bile duct cannulation and including the faecal metabolites, absorption is 82% after a low dose and 74% after a high dose at the minimum. Different oral absorption values (68% and 82%) have been used in competent authority reports based on different dossiers. The lower absorption value 68% obtained using bile duct cannulated animals is considered more accurate because enterohepatic circulation is excluded and it will be used for difenacoum. Difenacoum is widely distributed in the tissues, the main site of accumulation being the liver, the target organ. Elimination from the body is slow. The main elimination is *via* faeces, urine being only a minor route. Bile is an important route of excretion. During seven days after dosing, 37% of a low dose and 55% of a high dose is eliminated in faeces and approx. 2% in urine. Excretion is biphasic with half-lives of 3 and 118 days (Sorex Limited). During a five-day sampling, elimination half-lives of 55 and 42 hours were detected in females depending on dose level, and 45 and 31 hours in males, respectively (Activa/PelGar). After seven days of single dosing, four major metabolites were found in faeces and 2 to 5 in liver. Hydroxylation and glucuronidation are the main metabolic routes. The faecal metabolites accounted for 21% to 39% of the administered dose (range from different dossiers). Based on *in vitro* studies, dermal absorption value of 3% (pellets and grains) or 0.047% (wax block bait) is used for risk characterisation.

2.2.1.3. Health hazard of the active substance

Difenacoum is acutely very toxic by the oral and inhalation routes. Furthermore, it is justified to consider difenacoum very toxic also by the dermal route due to the overall mortality in one study and, because the lower confidence limit of the result of the acute toxicity test is below the threshold for classification in another study. It is not a skin or eye irritant. Difenacoum is not a skin sensitizer.

Repeated oral administration of difenacoum to rats resulted in marked increase in clotting time and haemorrhage in a wide range of tissues, with treatment related deaths due to massive haemorrhaging. Feeding rats at a dietary dose of up to 0.2 mg/kg bw/day for 90 days gave rise to clinical, haematological, biochemical and pathological findings indicative of toxic effects related to anticoagulation. No other adverse effects were observed. The NOAEL value could be established at 0.03 mg/kg bw/day. The above mentioned study reveals that repeated oral exposure to difenacoum results in toxic effects (lethal haemorrhages) giving cause to concern for serious damage to health by prolonged exposure. Furthermore, based on the results of the acute dermal and inhalation toxicity studies and route-to-route extrapolation, it is justified to assume a similar concern for serious damage to health by prolonged exposure through dermal and inhalation routes also.

Difenacoum was not mutagenic in bacterial cells, but the mutation frequency and chromosome aberrations were increased in mammalian cells *in vitro*. All *in vivo* genotoxicity tests were negative. Thus, it can be concluded that difenacoum is not classified as mutagenic.

Teratogenicity tests have been performed in two species. In competent authority reports, different NOAEL/LOAEL values were derived based on data provided in different dossiers. In the rabbit, the lowest LOAEL value for maternal toxicity is 0.001 mg/kg bw/day based on the increased haemorrhages in the kidneys (no NOAEL). A higher maternal NOEL/NOAEL value (0.005 mg/kg bw/day) was obtained based on prolongation of prothrombin time in another rabbit developmental toxicity study. The main difference in these studies is the length of the exposure period being 22 days or 13 days; the longer exposure period leads to the lower value. It is possible that the isomeric mixture of the compound has an impact, too. In both developmental toxicity studies, foetal effects (mainly skeletal) were observed but not considered treatment related. After a longer exposure period, higher incidences of skeletal variations were observed at two dose levels compared to controls, but the incidences were not dose dependent. After 13-day exposure, foetal effects (mostly vertebral and rib effects) were observed in both test and control groups including defects not previously seen in this strain or laboratory, but these effects were not dose related. The NOEL/NOAEL value for developmental toxicity is 0.01 mg/kg bw/day after 13-day exposure and 0.015 mg/kg bw/day after 22-day exposure. The NOEL/NOAEL for maternal toxicity in rats is 0.03 mg/kg bw/day. There was no evidence of embryotoxic or teratogenic potential following oral exposure of pregnant rats at 0.09 mg/kg bw/day (=NOEL/NOAEL for developmental toxicity).

In conclusion, clear developmental toxicity was not observed in rabbits or rats. However, difenacoum should be considered teratogenic to humans because it contains the same chemical moiety responsible for the teratogenicity of warfarin, a known human teratogenic agent, and it has the same mode of action that is a known mechanism of teratogenicity in humans. The

possible teratogenic effects of coumarin-related compounds can not be detected using the standard OECD 414 study design, because the exposure period has to be adjusted to correspond the critical periods in rat for the observed effects in humans. Furthermore, maternal bleeding has to be prevented, e.g. by vitamin K supplementation.

Effects on fertility have been studied in a rat multigeneration study (Activa/PelGar Task Force). In this study, dose levels had to be lowered twice during the course of the study due to extensive mortality. Regardless of the very low doses, it can be concluded that difenacoum does not have clear effects on fertility. However, there were indications of disturbed estrous cyclicity perhaps due to ovarian hormonal disturbance. Main findings related to fertility (irregular estrous cycles in treated animals in both generations and ovarian cyst at maternally toxic dose of 0.06 mg/kg bw/day in F0 females) did not affect the fertility index. No severe increase in postimplantation loss was observed. There are no studies on effects to fertility in the other dossier (Sorex Limited), but in analogy to teratogenicity and developmental toxicity, read-across from warfarin data is justified and new studies on fertility effects of difenacoum should not be performed due to ethical and animal welfare reasons. In the literature, there are no indications of adverse fertility effects associated to warfarin or vitamin K deficiency. Warfarin is not classified for fertility. It is considered that classification for fertility effects is not necessary for difenacoum and the possible effects on ovarian function are adequately covered by the risk phrase R48/23/24/25.

There are no studies on neurotoxicity. Other studies with difenacoum did not reveal any neurotoxic potential and there is no structural alert either.

Waiving of further long-term toxicity/carcinogenicity studies and repeated dose toxicity studies through other routes of exposure is justified based on scientific, ethical and animal welfare reasons.

2.2.1.4. Health hazard of the representative products

The representative products, Neosorexa pellets, MYOCURATTIN-Kanal-Diskus wax blocks, Roban wax blocks, or MYOCURATTIN-FCM-Granulat grain baits do not require classification for acute toxicity according to Directive 99/45/EC. The products are not irritating to skin or eyes. They are not skin sensitizers. However, due to the high acute toxicity of difenacoum and low NOAEL values, the principles for calculation of specific concentration limits for health hazards have been agreed.

2.2.1.5. AOEL (acceptable operator exposure level)

Different AOEL-values were derived and used in risk assessment in competent authority reports based on different dossiers. The lowest LOAEL in a repeated dose study, i.e. the teratogenicity study in rabbits, is chosen as the basis to establish the AOEL (there was no NOAEL). In this study, the maternal LOAEL was 0.001 mg/kg bw/day. Default assessment factors of 10 for inter-species variability and 10 for inter-individual variability are applied. Furthermore, due to the toxicological significance and uncertainty in the database, an additional safety factor of 3 for teratogenicity is used for all anticoagulant rodenticides according to the agreement during peer-review discussion. A further supportive argument for an additional assessment factor comes from the higher potency of the second generation anticoagulants compared to warfarin,

and from the much higher vulnerability of human foetuses to vitamin K deficiency compared to rodents. To extrapolate from LOAEL to NOAEL an assessment factor of 2 is considered justified due to the deep slope of the dose response curve. After correction for bioavailability of 68%, a NOAEL for MOE (0.00034 mg/kg bw/day) and an AOEL of 0.0000011 mg/kg bw/day are used for risk characterisation. These values are applied both to acute and repeated exposure scenarios.

2.2.1.6. Exposure and risk from use of the representative products

The exposure assessment was carried out on several ready-for-use formulation types: pellet baits (Neosorexa Pellets), grain-based granular baits (MYOCURATTIN-FCM-Granulat), and wax block bait (Roban wax blocks), all containing 50 mg/kg difenacoum. Both primary and secondary exposures were considered. Manufacturing of the active substance and formulation of the products are not covered. Based on worker monitoring data, protective measures are adequate. Assessment of repeated exposure from use of the products included the following tasks: decanting, filling of bait boxes and clean-up/disposal. Contrary to the primary exposure, secondary exposure is considered to be acute in nature.

Exposure assessment is based on measurements of a surrogate in simulated use conditions and on daily exposure frequencies according to a questionnaire answered by selected pest control companies in several EU countries. In primary exposure, the skin is the main exposure route, and only a small proportion of inhalation exposure to dust from decanting of pellets or grain baits is included in the total exposure. Inhalation exposure is not included for wax block formulation. Oral exposure is not considered relevant in primary exposure. Dermal absorption of 3% (pellets and grain baits) or 0.047% (wax block bait) and body weight of 60 kg for an adult is used for the calculations.

In competent authority reports, exposure and risk from the use of the representative products are calculated based on the dossiers submitted by the relevant applicants. Due to different data base (different repeated dose toxicity NOAEL/LOAEL-values and different bioavailability), different AOEL-values were set in competent authority reports. In this assessment report, the exposure to the products is compared to the lowest relevant repeated dose NOAEL/LOAEL- and AOEL-values identified in competent authority reports. This leads to higher risks for the products which were evaluated using a higher repeated dose NOAEL- and AOEL-values in competent authority reports.

In most cases, gloves must be used to reduce the exposure below the AOEL-value for trained professionals. For non-trained professionals and amateurs, the use is generally acceptable also without gloves.

Exposure from use of Neosorexa Pellets or MYOCURATTIN-FCM-Granulat grain baits to a trained professional, covering daily application and post-application tasks (79 daily exposures), results in 1.0×10^{-6} mg/kg bw/day systemic dose with protective gloves. The exposure is approx. 91% of the AOEL (0.0000011 mg/kg bw/day). Because non-trained-professionals (e.g. farmers) and amateurs are expected to handle much smaller amounts of baits daily, the exposure is at lower level than for the pest control operators. The calculated systemic dose (for 10 daily exposure) is 1.0×10^{-6} without protective gloves which is below the AOEL-value (91% of the

AOEL). Thus, it is concluded that non-trained professional/amateur use of pellet or grain baits does not result in unacceptable health risk.

Exposure for a trained professional covering daily application and post-application tasks (75 daily exposures, 60 loadings and 15 clean-ups) from use of wax block bait (Roban wax blocks) results in 1.3×10^{-7} mg/kg bw/day systemic dose with protective gloves. If protective gloves are worn, the risk is at acceptable level for Roban wax block, bait (12% of the AOEL-value of 0.0000011 mg/kg bw/day). Non-trained-professionals (e.g. farmers) and amateurs are expected to handle much smaller amounts of baits daily, and the exposure is at lower level than for the pest control operators. The calculated systemic dose for Roban wax blocks and 10 daily exposure is 1.2×10^{-7} without protective gloves which is below the AOEL-value (11% of the AOEL). It is concluded that non-trained professional/amateur use of wax block baits does not result in unacceptable health risk. See Appendix III for a summary of risk characterisation for users of the representative products.

Exposure calculations for MYOCURATTIN-Kanal-Diskus, a wax block containing 75 mg/kg difenacoum, are not done. The dermal absorption value of 3 % used in the CAR may overestimate the exposure taking into account that the dermal absorption value was much lower (0.047%) for the wax block formulation containing 50 mg/kg difenacoum. Calculations using a product specific dermal absorption value are expected to indicate acceptable risks.

Secondary exposure from transient mouthing of the products exceeds the reference value (0.0000011 mg/kg bw/day), both with the assumption of 0.01 g and 5 g of product ingested by infants. This indicates that infants are at significant risk of poisoning.

Assessment of combined exposure is not necessary, because indirect exposure via the environment is considered negligible.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Difenacoum is only slightly soluble in water in neutral conditions, and it is hydrolytically stable. Difenacoum undergoes rapid phototransformation in water (half-life about 8 hours or less). Two applicants did not identify transformation products, because individual transformation products were formed less than 10% of the active substance added. In the photolysis study of Activa/Pelgar Brodifacoum and Difenacoum Task Force two breakdown products above 10% were detected, but not chemically identified. Possible structures of degradation products are presented in Doc IIIA.7.1.1.1.2. Because the photodegradation is regarded as a minor removal process for difenacoum and the exposure to water is low no further characterization of metabolites was deemed necessary. Difenacoum is not volatile.

Difenacoum is not readily or inherently biodegradable. Difenacoum degrades slowly under aerobic conditions in soil, with a measured DT50 of 439 days. Photolysis may contribute to the degradation in soil, but in the lack of experimental evidence, soil photolysis can not be taken into account.

The QSAR K_{oc} value of 1.8 x 10^6 is used in the risk assessment instead of the experimentally derived K_{oc} values, because they were regarded unreliable. The K_{oc} values were determined with the HPLC method and although the studies *per se* were regarded valid, the test method appeared to be unsuitable for difenacoum. The HPLC method (OECD 121) is not an actual study with measurements in real soil, but only an estimation based on the comparison of test substance to reference substances under artificial system, and hence there may be more uncertainties than in the adsorption/desorption batch-test (OECD 106). The experimentally derived K_{oc} values were inversely related to pH, so that high values were obtained in acidic conditions (K_{oc} of 426 579 at pH 3-4) and low values in neutral or alkaline conditions (17-165 at pH 7-8.5). The experimentally derived K_{oc} values are not supported by the physical and chemical properties of difenacoum. Difenacoum is a large aromatic molecule with two polar groups which can potentially ionize at environmental relevant pH. Difenacoum has also a low water solubility and a high log K_{ow}. The HLPC-method gives quite low Koc value suggesting that ionized form of difenacoum will not have great affinity to organic matter. Although difenacoum is a weak acid with probably two dissociable sites, it might not be in ionized form with low adsorption in natural environment, or ionizable form might behave like a neutral form if the charge is shielded by the large molecule size. Also comparison to similar anticoagulant molecules supports the expert view that due to the intrinsic properties of these molecules the adsorption to particles is probable. One applicant has also experimental data which show that difenacoum is not mobile in soil, as concentrations in leachate from column leaching studies conducted with both the active substance and the product were non-determinable. Difenacoum is therefore not expected to contaminate groundwater.

Difenacoum has a considerable bioaccumulation potential in aquatic and terrestrial organisms. One applicant submitted a fish bioconcentration test, but it was not considered as acceptable by the RMS. The waiving of fish bioconcentration test was accepted, because the test was judged not possible to perform technically, and because an estimated BCF value could be used in the risk assessment. The calculated BCFs range from 9010 to 477 729 clearly not passing the Annex I inclusion criteria of the Directive, i.e. 100 for substances which are not readily biodegradable. In the TNsG on Annex I Inclusion, it is stated that "An active substance with a BCF > 5000 shall not be included in Annex I". It is further said that "an active substance shall not be included in Annex I if the BCF related to fat tissues in non-target vertebrate is above 1 unless it is clearly established in the risk assessment that under field conditions no unacceptable effects occur, either directly or indirectly, after use of the biocidal product according to the proposed conditions of use." The calculated BCFs estimate bioconcentration in the whole animal and not in the fat tissue, so BCF for difenacoum in fat tissue of the non-target vertebrates is unknown. The risk assessment indicates that accumulation of difenacoum in predators results in unacceptable effects when compared with the environmental acceptance criteria given in the Directive and TNsG on Annex I Inclusion.

2.2.2.2. Effects assessment

Difenacoum is very toxic to fish, aquatic invertebrates and algae. Fish is the most sensitive species. The toxicity in fish is based on the inhibition of blood clotting, whereas mode of action in the invertebrates and algae is unknown. The $PNEC_{water}$ is 0.06 µg/l based on the LC50 for the rainbow trout. Difenacoum did not inhibit growth or respiration of aquatic microbes. The PNEC for sewage treatment plant (STP) micro-organisms is 2.3 mg/l (Sorex Limited) or

0.48 mg/l (Activa/PelGar Task Force). In the absence of any ecotoxicological data for sediment-dwelling organisms, the $PNEC_{sediment}$ was calculated using the equilibrium partitioning method. The $PNEC_{sediment}$ is 2.51 mg/kg (wet weight).

Difenacoum caused no toxic effects in the acute earthworm test and a $PNEC_{soil}$ of 0.877 mg/kg wet weight was determined. Because only one soil test was available, the $PNEC_{soil}$ of 2.04 mg/kg wet weight was derived with the equilibrium partitioning method (EPM). Because the experimentally derived $PNEC_{soil}$ is lower, it is used in the risk assessment of the Activa/Pelgar Task Force. The EPM derived $PNEC_{soil}$ of 2.04 mg/kg wet weight was used for the applicants which did not have any terrestrial data. Difenacoum is moderately toxic to very toxic to birds depending on the particular test and exposure duration. In the avian reproduction study of Sorex Limited difenacoum did not affect reproduction at or below 0.1 mg/kg diet. On the other hand, several dose related effects were detected in the reproduction test of Activa/Pelgar Task Force: increased adult mortality, increased mortality of 14-day old hatchlings, increased liver and spleen weights in adult females, a declining trend in number of eggs laid/hen/day, declining trend in viability of eggs. The two reproduction tests followed different guideline and difenacoum was mixed in food in the first test and in water in the second test. Due to methodological deficiencies the latter test is not considered to represent the worst case, and therefore the $PNEC_{oral}$ of birds was derived from the dietary test for the Activa/Pelgar Task Force. Difenacoum is very toxic to mammals, and rats seem to be particularly susceptible. $PNEC_{oral}$ for birds and mammals has been used in the risk characterisation of primary and secondary poisoning. For the applicants Sorex Limited and Hetschke & Sawatzki KG, the avian $PNEC_{oral}$ is 3 µg/kg in food or 0.3 µg/kg bw/d as a dose. For the applicant Activa/PelGar Task Force the avian $PNEC_{oral}$ is 0.5 µg/kg in food or 0.1 µg/kg bw/d as a dose. The $PNEC_{oral}$ for mammals is 7 µg/kg in food or 0.3 µg/kg as a dose. (Identical test result was obtained in all three dossiers, and hence the $PNEC_{oral}$ is also identical for the three applicants.)

In the dossier of Activa/PelGar Task Force two major faecal metabolites were identified as isomers of hydroxylated difenacoum and two other major metabolites were characterised as isomers of difenacoum-based structure which formed glucuronide conjugates. Other faecal metabolites each accounted for <4%. As no information on toxicity of these four major metabolites is available and the 4-hydroxy-coumarin moiety is still present and thus the metabolites could be potent as anticoagulants, it is assumed that the toxicity of metabolites is comparable to the parent compound. In the dossiers of Sorex Limited and Hentschke & Sawatzki KG metabolites of difenacoum released by rats via faeces may be considered to be of ecotoxicological relevance than the parent compound itself. The polar metabolites, although not identified, may generally be considered as less toxic (related to mode of action as anticoagulant) by extrapolation from closely related anticoagulants. Also the concentrations of individual polar metabolites in the environment are not very significant; the less polar substances may be judged as environmentally insignificant since constituting less than 10% of applied parent compound.

2.2.2.3. PBT assessment

Difenacoum potentially fulfils the PBT criteria. Difenacoum is not readily or inherently biodegradable and half-life in marine or freshwater sediment is expected to be more than 180 days or 120 days, respectively. The assumption is based on the available half-life in one soil which was 439 days. Difenacoum is also hydrolytically stable, but photolytic degradation in

water is rapid. The photolytic degradation is not regarded as a major transformation pathway in nature. Difenacoum has a high potential for bioaccumulation based on the calculated log K_{ow} and BCF. Based on both the ecotoxicological and toxicological data, difenacoum fulfils the T criterion. It is likely that the B criteria cannot be refined with further testing: it may not be technically possible to conduct a valid fish bioconcentration test. According to the TGD the refinement of the PBT assessment is started by clarifying the potential for persistency first. If the participant wishes to challenge the P criteria, a water/sediment degradation study is required. Nevertheless, difenacoum is not a candidate for a persistent organic pollutant (POP), as it does not have a potential for long-range atmospheric transport. According to the TNsG on Annex I Inclusion, substances which fulfil the PBT or vPvB criteria should not be included in Annex I unless releases to the environment can be effectively prevented.

2.2.2.4. Risk characterisation

Aquatic compartment (incl. sediment)

The PEC/PNEC ratios for water, sediment and STP micro-organisms are below 1 indicating that difenacoum does not cause unacceptable risk to aquatic organisms, sediment-dwelling organisms or biological processes at the sewage treatment plant. The PEC/PNEC ratios are calculated for the proposed normal use together with a realistic worst-case scenario. Also accumulation in the sediment is regarded to be low, although difenacoum is not readily biodegradable and it is expected to degrade slowly in the sediment. It is neither expected that difenacoum would contaminate groundwater.

Atmosphere

Difenacoum is not expected to partition to the atmosphere to any significant extent due to low vapour pressure and Henry's Law constant. Difenacoum has a potential for rapid photo-oxidative degradation in the air (half-life about two hours). Difenacoum is not expected to have a potential for long-range atmospheric transport or contribute to global warming, ozone depletion or acidification on the basis of its physical and chemical properties.

Terrestrial compartment

No risk was identified in soil in scenarios in and around buildings or waste dump. Ten years application of sewage sludge to soil did neither result in the risk. The only scenario where risk was identified was the open area scenario where the PEC/PNEC ratio was 1.7. The ratio was obtained by dividing the PEC of 0.346 mg/kg with a $PNEC_{soil}$ of 2.04 mg/kg. Because the $PNEC_{soil}$ was derived with the equilibrium partitioning method and log $K_{ow} > 5$, the PEC/PNEC ratio was multiplied with a factor of 10 according to the TGD, Part II section 3.6.2.1.

Sorex Limited was the only applicant supporting the open area use and has agreed to provide an earthworm reproduction test for the product authorisation phase in order to refine the risk in the open area use. The reason for not requiring a short-term study is that difenacoum is expected to be more toxic in the long-term exposure (at least this is the case for the vertebrates). The long-term study allows the use of a lower assessment factor in the derivation of PNEC compared to the short-term data. No tests on the soil micro-organisms or plants are required,

because difenacoum is not expected to be particularly toxic to them on the basis of the mode of action and available data (Activated sludge, respiration inhibition test).

According to the testing strategies in the TNsG on Data Requirements, an adsorption/desorption batch equilibrium test on soils and an aerobic soil degradation test should be required in order to refine the PEC. However, the studies are not required as adsorption and degradation are not taken into account in the calculation of PEC according to the rodenticide emission scenario document (ESD).

An active substance shall not be included in Annex I if the DT90 is over one year or the DT50 is over three months in the soil field tests or if non extractable residues exceed 70% of the initial dose after 100 days with a mineralization rate less than 5% in 100 days (TNsG on Annex I Inclusion). The latter criteria cannot be evaluated for difenacoum as non-extractable residues have not been determined in the only available study. Comparison of the DT50 of 439 days from a laboratory test to the persistence criteria indicates that the persistence half-life of difenacoum exceeds this criterion.

Primary and secondary poisoning

According to the risk calculations the proposed normal use of difenacoum causes unacceptable risk for primary and secondary poisoning of non-target vertebrates. However, the risk for primary poisoning is assumed to be negligible in the ESD if the rodenticidal baits are used according to the label instructions. In the aquatic food chain (fish-eating birds and mammals) risk for secondary poisoning is considered insignificant. In the terrestrial food chain secondary poisoning is possible via contaminated soil invertebrates and rodents, and the latter animals are the most likely source for difenacoum residues in raptorial birds and mammalian predators. Not only the risk characterisation shows risk for secondary poisoning, but also the published laboratory studies confirm bioaccumulation of difenacoum in the owls. Bioaccumulation of difenacoum in predators has been shown in the measurements of difenacoum residues in the animal carcasses found from the field in United Kingdom. The target organ for difenacoum is liver and difenacoum residues in the carcasses have been measured from the liver. In one laboratory study highest residues were measured in the liver, and residues in other tissues including the fat tissue were low. Owls exposed to difenacoum showed variable effects from no foreseeable effects to death. Other observed effects were increased coagulation times and haemorrhages. The effects disappeared gradually after the end of exposure. Population level effects of difenacoum have not been studied.

In the laboratory studies, the owls fed entirely or mostly on poisoned rodents which may not be probable in the field conditions. The carcasses found from the field were diagnosed to have died to other reason than difenacoum and difenacoum residues were assumed to be sublethal. It is, however, possible that sublethal difenacoum residues have contributed to the death of predators. Reproductive effects of difenacoum in avian or mammalian predators or scavengers have not been studied in the laboratory or in field experiments. Dose-related effects on the reproduction were observed in Japanese quail in the reproduction study of the Activa/PelGar Task Force. The NOEC of 0.31 mg/l drinking water and NOEL of 58 µg/kg bw were determined in this study. In the reproduction study of Sorex Limited no dose-related reproductive effects were observed in Japanese quail resulting in the NOEC of > 0.1 mg/kg diet

and NOEL of > 0.01 mg/kg bw/d. Higher concentrations were not tested. The residues in the liver were not measured in either test, and hence the comparison to the monitoring data is difficult. The residue levels measured from dead barn owls ranged from 0.05-0.2 mg/kg in liver.

In conclusion difenacoum does not fulfil the environmental acceptance criteria due to bioaccumulation and unacceptable effects in the non-target vertebrates.

2.2.3. List of endpoints

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

3. DECISION

3.1. Background to the Decision

Difenacoum has been evaluated as a rodenticide in the following use situations: in and around buildings, in sewers, in open areas and around waste sites. The target species are brown rat, black rat and house mouse.

Difenacoum is sufficiently effective against both rats and mice to be included in Annex I. Resistance to difenacoum occurs in some Member States, but so far the resistance is not regarded as unacceptable. In order to prevent the development and spreading of resistance, difenacoum should be used only by trained professionals. Difenacoum should not be used continuously. The rodent control strategy should also include habitat management where the access of rodents is physically prevented. The susceptibility of rodents to difenacoum should be ensured before start of the baiting. After the control campaign, it should be ensured that a complete elimination of rodents was achieved. In areas where difenacoum resistance has been discovered, difenacoum should not be used. In these areas, more potent anticoagulants or non anticoagulant rodenticides should be used.

It is recognised that anticoagulants like difenacoum 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 non-biocidal alternatives are not available.

Based on the assessment of data on the active substance and the representative products containing 50 mg/kg difenacoum, health risks for the users of the biocidal products are at an acceptable level if principles of good working practice are applied and use instructions and recommendations on the label of the product are respected. The health risks for wax block bait product containing 75 mg/kg difenacoum (MYOCURATTIN-Kanal-Diskus) are expected to be acceptable when calculated using a product specific dermal absorption value. The accidental ingestion of baits poses a risk to infants. Adequate measures for protection and risk mitigation have to be applied during use to control especially the risk from secondary exposure.

The environmental risk assessment shows that difenacoum does not cause unacceptable risk in the aquatic environment or in the atmosphere. Difenacoum is neither expected to accumulate in sediment nor contaminate groundwater. In the terrestrial environment, difenacoum causes risk to non-target soil organisms only in the open area scenario. The refinement of risk assessment by using experimental data to derive the $PNEC_{soil}$ is expected to lower the PEC/PNEC below 1, because the current $PNEC_{soil}$ is derived with the equilibrium partitioning method. Difenacoum is persistent and exceeds the Annex I inclusion criteria for soil. On the other hand, proposed use of difenacoum may not result in unacceptable accumulation in soil because the baits should be deployed in the tamper resistant bait boxes and uneaten baits should be collected after the control campaign.

Difenacoum poses an unacceptable risk for primary and secondary poisoning of birds and other non-target mammals. The risk for primary poisoning can be reduced by deploying baits so that they cannot be reached by the non-target animals. The risk for secondary poisoning is more

difficult to control, as poisoned rodents may be available for predators for several days after intake of difenacoum. The use of difenacoum inside the buildings may reduce the secondary poisoning risk, but does not exclude it as the exposed rodents may move out from the building. The secondary poisoning can be excluded only in fully enclosed spaces where rodents cannot move to outdoor areas or to areas where predators may have access. When using difenacoum as a rodenticide all possible measures have to be taken in order to minimize secondary poisoning of the non-target animals. The measures include use of tamper resistant bait boxes, collection of unconsumed baits after termination of the control campaign and collection of dead rodents during and after the control campaign. Only professional users, i.e. trained rodent control operators, are expected to use rodenticidal baits according to the instructions so that the risk for secondary poisoning is minimised.

Difenacoum is a potential PBT substance and such substances should not be included in Annex I unless releases to the environment can be effectively prevented. The direct releases of difenacoum to the environment can be minimised by using the ready-for-use baits and following the measures described in connection to the secondary poisoning.

The representative products in the risk assessment were ready-for-use products and risks associated with other type of formulations have not been evaluated. The risk assessment has been done for products containing 50 mg/kg. The health risks of the representative products are considered acceptable with the use of PPE. The health risks are expected to be acceptable also for the wax block containing 75 mg/kg difenacoum when product specific dermal absorption values are used in calculations.

According to the Annex I inclusion criteria referred to in Article 10 of the Directive and TNsG on Annex I inclusion, difenacoum should not be included in Annex I. However, in the decision making also benefits of using the active substance in the biocidal products have to be considered (Paragraph 96 in Annex VI of the Directive). Rodent control is needed to prevent disease transmission, contamination of food and feedingstuffs, structural damage and social abhorrence. Currently anticoagulants are the dominating substances in rodent control. Fourteen rodenticides are included in the review programme of the existing biocidal substances, and nine of these substances are anticoagulants, two are gases and three are non-anticoagulants. It is concluded that difenacoum is needed as a rodenticide for human hygiene and public health reasons. It enables effective control of the target rodents and it can be used against rats and mice which are resistant to the first generation anticoagulants such as warfarin and coumatetralyl. In this exceptional case the benefit should take precedence over the risks and difenacoum should be included in Annex I.

Difenacoum is suggested as a candidate for the comparative assessment due to the potential PBT properties, unacceptable risk for secondary poisoning of the non-target vertebrates and risk for secondary exposure of humans. A more detailed risk benefit analysis should be made as a part of the comparative assessment when more information is available on alternative substances.

3.2. Decision regarding Inclusion in Annex I

Difenacoum shall be included in Annex I to Directive 98/8/EC as an active substance for use in product-type 14 (rodenticides), subject to the following specific provisions. The active substance difenacoum, as manufactured, shall have a minimum purity of 960 g/kg. The minimum purity is supported by the analytical data (5-batch analysis) of Sorex Limited. A higher minimum purity of 995 g/kg is supported by the analytical data of PelGar International Ltd. Most of batches used in the toxicity and ecotoxicity tests are of purity with reference to these specifications.

In view of the fact that the active substance characteristics render it potentially persistent, liable to bioaccumulate and toxic, the active substance is to be subject to a comparative risk assessment in accordance with the second subparagraph of Article 10(5)(i) of Directive 98/8/EC before its inclusion in this Annex is renewed.

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

(1) The nominal concentration of the active substance in the products shall not exceed 75 mg/kg and only ready-for-use baits shall be authorised.

(2) Products shall contain an aversive agent and, where appropriate, a dye.

(3) Products shall not be used as tracking powder.

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

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

- The use of appropriate personal protective equipment should be advised in the use instructions.
- As professional users are likely to be exposed more often, products containing difenacoum may be used by professional users if data are provided to show that calculated occupational exposure based on the operator exposure study, is acceptable.
- The restriction of products to specific areas and manners of use and also restrictions of products to professionals or trained professionals only, should be considered.
- The size of the package placed on the market should be proportionate to the duration of the treatment and appropriate to the pattern of use of particular user groups.
- Product design and use restrictions should be optimised in order to ensure sufficient efficient rodent control while at the same time minimizing the risk for primary

poisoning. This could include the use of tamper resistant bait boxes and the need to secure the baits so that rodents cannot remove the bait from the bait box.

- When tamper-resistant bait stations are used, they should be clearly marked to show that they contain rodenticides and that they should not be disturbed.

- Difenacoum baits should not be placed where food, feedingstuffs or drinking water could be contaminated.

- In case no standard safety phrases are required on the product label, adequate safety instructions should be provided in the use instructions.

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 protect humans, animals or the environment:

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

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

- Unless under the supervision of a pest control operator or other competent person, do not use anticoagulant rodenticides as permanent baits.

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

- Keep out of the reach of children.

This last safety precaution should always be carried on the label 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 campaign. 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 difenacoum should not be used in an area where resistance to this substance is suspected.

- The authorisation holder shall report any observed resistance incidents to the Competent Authorities or other appointed bodies involved 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 indicating the first measures to be taken in case of poisoning must be made available alongside the baits.

3.4. Requirement for further information

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the inclusion of difenacoum in Annex I to Directive 98/8/EC. However, in order to refine the risk assessment for the terrestrial compartment in the open area use Sorex Limited and Hentschke & Sawatzki KG will provide an earthworm reproduction test for the product authorisation phase. Data on dermal absorption for the wax block product containing 75 mg/kg difenacoum (Hentschke & Sawatzki KG) are required for the product authorization phase. The Activa/Pelgar Task Force has not submitted some studies that are required for the PT 14 and therefore the studies are required for the product authorisation phase.

- Analytical data to prove the isomeric composition and impurity profile from the task force member Activa (A2.8).

- For appearance ownership of data, for the technical substance, should be demonstrated or a study should be submitted (A3.3).

- A validated method for the analysis of difenacoum in animal and human tissues (A4.2d).

- Validation data for the analytical method for determination of residues of difenacoum in meat and oil-seed rape (food/feeding stuffs) (B4.2e).

- Validation data for analytical method for determination of difenacoum in sediment (based on the analysis method for difenacoum in soil) (A4.2c).

3.5. Updating this Assessment Report

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

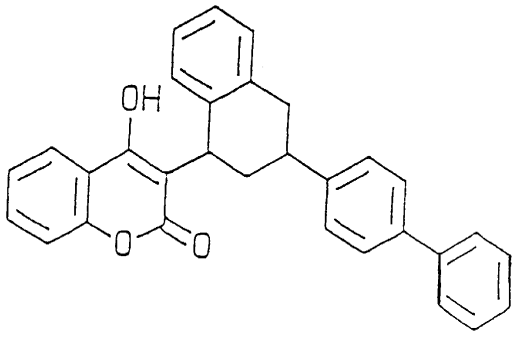
Appendix I: List of endpoints

Note: The owner of data is marked before or after endpoints where relevant: S = Sorex Limited, HS = Hentschke & Sawatzki KG, A/P = Activa/PelGar Brodifacoum and Difenacoum Task Force. In case of several values in each toxicological endpoints, the value used in risk assessment is indicated in bold. Concerning the environmental risk assessment two values per endpoint are given in most cases. Data owned by Sorex have been used for Sorex and Hentschke & Sawatzki and data owned by Activa/PelGar have been used for the Activa/PelGar Task Force. The different values do not change the results or conclusions of the risk assessment.

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

Active substance (ISO Common Name)	Difenacoum
Product-type	PT 14: Rodenticides
Rapporteur Member State	Finland

Identity

Chemical name (IUPAC)	3-(3-biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphthyl)-4-hydroxycoumarin
Chemical name (CA)	2*H*-1-Benzo pyran-2-one, 3-(3-[1,1'-biphenyl]-4-yl-1,2,3,4-tetrahydro-1-naphthalenyl)-4-hydroxy-
CAS No	56073-07-5
EC No	259-978-4
Other substance No.	514 (CIPAC No)
Minimum purity of the active substance as manufactured (g/kg or g/l)	960 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None.
Molecular formula	$C_{31}H_{24}O_3$
Molecular mass	444.5
Structural formula	

Physical and chemical properties

Melting point (state purity)	211 – 215 °C (Purity: 98.7% w/w) (S) An endotherm at 226.3 °C, melting is proposed. (Purity: 99.7% w/w) 216.3 – 226 °C, melting (with signs of degradation) (99.7% w/w) (A/P)
Boiling point (state purity)	No boiling point before start of decomposition. (S) No boiling point detected, In tests up to the temperature of 250 °C. (99.7% w/w) (A/P)
Temperature of decomposition	>300 °C (96.5%) (S) >250 °C (99.7%) (250 °C was the highest temp. of test) (A/P)
Appearance (state purity)	White fine powder at 20 °C (Purity: 98.7% w/w), off-white for technical grade. (S) Solid off-white powder (99.7%) (A/P) Buff/beige fine powder (technical grade, >90%), (A/P)
Relative density (state purity)	1.27 at 20.5 °C (Purity: 98.7% w/w) (S) 1.1363 at 20 °C (Purity: >99% w/w) (A/P)
Surface tension	Not determined. Not applicable.
Vapour pressure (in Pa, state temperature)	1.9×10^{-11} Pa, with total error of x 352.5, at 25 °C (98.7%), (computer-based estimation). This can be expressed also as a range of **6.7×10^{-9}** – 5.4×10^{-14} Pa. The high-end value was used for Henry's law constant. (S) < 5×10^{-5} Pa at 45 °C (99%), an estimation. (A/P)
Henry's law constant (Pa m^3 mol^{-1})	1.75×10^{-6} Pa m^3 mol^{-1} at pH 7 4.9×10^{-8} Pa m^3 mol^{-1} at pH 9 (S) <0.046 Pa m^3 $mole^{-1}$, an estimation (A/P)
Solubility in water (g/l or mg/l, state temperature)	pH 4: <0.05 mg/l at 20 °C (97.8%) (S) pH 5.1: ≤ 0.05 mg/l 20 °C (99.7%) (A/P) pH 7: 1.7 mg/l at 20 °C (S) pH 6.5: 0.43mg/l at 20 °C (A/P) pH 9: 61 mg/l at 20 °C (S) pH 8.9: 3.72 mg/l at 20 °C (A/P)
Solubility in organic solvents (in g/l or mg/l, state temperature)	Purity: 96.3% w/w Temperature: 20 °C Acetone: 7.6 g/l Propan-2-ol: 1.5 g/l Ethylacetate: 3.7 g/l Toluene: 1.2 g/l Methanol: 1.2 g/l Hexane: 12.1 g/l Dichloromethane: 19.6 g/l (S) Purity: 99.7% w/w

	Temperature: 20 °C Toluene : 1.49g/l Ethyl acetate: 3.60g/l Methanol: 1.00g/l Acetone: 8.12g/l Dichloromethane: 17.39 g/l (A/P)
Stability in organic solvents used in biocidal products including relevant breakdown products	Not applicable
Partition coefficient (log K_{OW}) (state temperature)	7.6 (estimated using a computer atom/fragment contribution method) (S) 7.62 (a QSAR estimation) The experimental information available on difenacoum suggests that it may be beyond the performance ranges of the experimental tests for log K_{ow}. (A/P) The estimation concerns the undissociated species.
Dissociation constant	pKa value 4.84 (purity: 96.2%) (S) pKa value 4.5 ± 1.00 (a QSAR estimation) (A/P)
UV/VIS	Wavelength of peak (nm) 310.6 and 259.4 $\varepsilon_{310.6}$ = 17 100 $M^{-1}cm^{-1}$ $\varepsilon_{259.4}$ = 46 600 $M^{-1}cm^{-1}$ (98.7%) (S) Wavelength of peak (nm) 308 and 259 ε_{308} = 12926 l/mol.cm^{-1} ε_{259} = 28515 l/mol.cm^{-1} (98.8%) (A/P)
Flammability	Not highly flammable (96.18%) No self-ignition at temperatures up to melting point (211-215 °C) (S) Not highly flammable (>99%) No self-ignition at temperatures up to 215 °C, high end temperature of the test (99%) (A/P)
Explosive properties	Not explosive (based on expert statement) (S) Not explosive (based on a statement) (A/P)
Oxidizing properties	Not oxidizing (96.18%) (S) Not oxidizing (based on studies and a statement) (>99%) (A/P)

Classification and proposed labelling

with regard to physical/chemical data	None
with regard to toxicological data	T+; R26/27/28, Repr. Cat. 1; R61,T; 48/23/24/25
with regard to fate and behaviour data	N; R53
with regard to ecotoxicological data	N; R50
specific concentrations limits for the human and environmental classification	C ≥ 2.5% T+, N; R26/27/28-48/23/24/25-61-50-53 0.5% ≤ C < 2.5% T+, N; R26/27/28-48/23/24/25-61-51-53

	0.25% ≤ C< 0.5% T+, N; R26/27/28-48/23/24/25-51-53 0.025% ≤ C< 0.25% T ; R23/24/25-48/20/21/22-52-53 0.0025% ≤ C < 0.025% Xn; R20/21/22
	No classification of products containing 50 mg/kg or 75 mg/kg difenacoum would be necessary according to Directive 1999/45/EC. However, specific concentration limits of difenacoum have been agreed by the Technical Committee on Classification and Labelling.

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	Difenacoum quantified in technical grade material by HPLC with u.v. detection at 254 nm using an internal standard. (S, A/P)
Impurities in technical active substance (principle of method)	Impurities in technical grade material quantified by HPLC with u.v. detection using either an internal or external standard. (S, A/P)

Analytical methods for residues

Soil (principle of method and LOQ)	After extraction of the soil samples by acidified dichloromethane: methanol, followed by filtration and evaporation quantification is done by HPLC with MS/MS detector and external standardisation. The method has been acceptably validated for samples of soil containing difenacoum at levels of 0.01-0.1 mg/kg. LOQ is 0.01 mg/kg. (S) After extraction of the soil samples by chloroform:acetone, concentrated extracts are purified with a Florisil-sodium sulphate column. Quantification is done by HPLC-DAD detector. The method has been acceptably validated for samples of soil containing difenacoum at levels of 0.016, 0.063 and 0.158 mg/kg. LOQ is 0.0214 mg/kg. (A/P)
Air (principle of method and LOQ)	Not relevant, due to the low vapour pressure of difenacoum
Water (principle of method and LOQ)	Extraction of difenacoum from surface water involves acidification of the surface water samples, followed by extraction with dichloromethane. Quantification is done by LC-MS/MS in positive chemical ionisation mode. LOQ is 0.01 µg/l. (S & HS) The test method for determination of difenacoum in drinking, ground and surface waters is based on extraction by dichloromethane. Quantification is done by LC-MS/MS (both SIM and SMR mode). LOQ is 0.05 µg/l for drinking water and groundwater and 0.5 µg/l for surface water. (A/P)
Sediment (principle of method and LOQ)	Extraction of difenacoum from sediment involves a double extraction with acidified dichloromethane:methanol (4:1, v/v), followed by a filtration step. Quantification is done by LC-MS/MS in positive chemical ionisation mode. LOQ is 0.01 mg/kg.

	(S)
Body fluids and tissues (principle of method and LOQ)	Samples are extracted with acetonitrile, then quantified using HPLC with fluorescence detection and an external standard. LOQ is 0.01 mg/kg rat liver. (S)
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Method of residue analysis for cucumber, wheat flour, citrus and oilseed rape has been tested. Four different pre-treatment methods have been developed depending on the specimen's properties (water, fat, and acid content). The purified extracts are analysed for residues of difenacoum by LC-MS/MS. LOQ is 0.01 mg/kg. (S, HS) Method of residue analysis for cucumber, wheat and lemon has been validated acceptably. The purified extracts are analysed for residues of difenacoum by LC-MS. LOQ is 0.01 mg/kg. (A/P)

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Peak plasma level reached 4-24 h after dosing. 82% of a low dose and 74% of a high dose absorbed within 168 h (faecal metabolites included). This amount is expected to be the minimum, because the measured metabolite:difenacoum ratio is at 24 h, and it is expected to increase between 24 and 168 h. (S) Bile duct cannulated animals: **68%** after a single 0.1 mg/kg dose (bile, urine, liver and carcass included). (A/P)
Rate and extent of dermal absorption:	The estimated dermal absorption in humans is **3%** for the Neosorexa Pellets, based on an *in vitro* study using human skin. (S) **0.047%** for the Roban wax block, during 24 h after 8 h exposure in an *in vitro* study with human skin. (A/P)
Distribution:	Widely distributed; highest residues in liver
Potential for accumulation:	Yes, long half-lives for elimination and binding to liver
Rate and extent of excretion:	Slow, biphasic with half-lives of 3 and 118 days. (S). During a five-day sampling, elimination half-lives of 55 and 42 hours in females depending on dose level, and 45 and 31 hours in males, respectively (A/P). Within seven days 37-55% eliminated in faeces and less than 3% in urine
Toxicologically significant metabolites	21-39% of the administered dose is as metabolites in faeces (hydroxylated difenacoum and glucuronide conjugates identified by A/P). 2-5 unidentified metabolites found in liver. Metabolism is assumed to lower the anticoagulant potency significantly

Acute toxicity

Rat LD_{50} oral	1.8 mg/kg bw to the male rat; 2.6 mg/kg bw to the female rat.
Rat LD_{50} dermal	63 mg/kg bw (95% confidence limits 34-85) to the male rat. Two out of five deaths at 20 mg/kg bw (males)

	51.54 mg/kg bw (females)
Rat LC_{50} inhalation	3.646 - 5.848 µg/l/4 h, head-only (S) 16.27-20.74 µg/l/4 h, nose only (A/P)
Skin irritation	Not irritating
Eye irritation	Not irritating
Skin sensitization (test method used and result)	Negative (Magnusson and Kligman test and Buehler). Overall conclusion: Not a skin sensitizer

Repeated dose toxicity

Species/ target / critical effect	Species/ target / critical effect Rat (90-day); prothrombin time prolongation, kaolin-cephalin time prolongation, haemorrhage.
Lowest relevant oral NOAEL / LOAEL	0.03 mg/kg bw/day
Lowest relevant dermal NOAEL / LOAEL	-
Lowest relevant inhalation NOAEL / LOAEL	-

Genotoxicity	*In vitro:* positive result in mammalian gene mutation test and in mammalian chromosome aberration tests. *In-vivo*: Negative results in micronucleus tests and in UDS-tests. Conclusion: No genotoxic effects

Carcinogenicity

Species/type of tumour	Study waived
lowest dose with tumours	-

Reproductive toxicity

Species/ Fertility target / critical effect	Rat: Haemorrhages in parents, no clear effects on fertility, but some indications of possible effects on ovarian function (changes in oestrus cycle and ovarian cysts). (A/P)
Lowest relevant reproductive NOAEL / LOAEL	No NOEL
Species/ Developmental target / critical effect	Rabbit: increased clotting time and haemorrhage in dams; no clear developmental toxicity in fetuses (some defects or skeletal variations observed without dose-dependence). Rat: Haemorrhages in dams; no effects in fetuses
Lowest relevant developmental NOAEL / LOAEL	Rabbit: 13-day exposure (gestation days 8-20) (S): NOEL/NOAEL: 0.005 mg/kg bw/day for maternal toxicity NOEL/NOAEL 0.015 mg/kg bw/day for teratogenicty

	and embryotoxicity 22-day exposure (gestation days 7-28)(A/P): LOAEL: **0.001 mg/kg bw/day** for maternal toxicity NOEL/NOAEL: 0.01 mg/kg bw/day for teratogenicity and embryotoxicity Rat: NOEL/NOAEL: 0.03 mg/kg bw/day for maternal toxicity NOEL/NOAEL: 0.09 mg/kg bw/day for teratogenicty and embryotoxicity

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	Not available. No evidence for neurotoxic potential from other studies
Lowest relevant developmental NOAEL / LOAEL.	-

Other toxicological studies

.....	-

Medical data

Medical Doctor's Report on Worker Monitoring	Routine monitoring of workers (industrial users) producing the active substance and formulating products has been carried out for the last forty years. Between June 1981 and September 1982, three poisoning incidents occurred with successful recovery. With the exception of these incidents, routine monitoring has shown no clinical effects in any workers. During this time there has been no evidence of allergy, sensitisation or any other abnormal effects induced by repeated and continual exposure to these anticoagulant rodenticides. (S) Regular health screening of manufacturing workers in one facility producing anticoagulant rodenticides, including difenacoum, since 1970's have not revealed poisoning cases oe any other adverse health effect related to difenacoum. (A/P)

Summary	Value	Study	Safety factor
ADI (if residues in food or feed):	Not applicable		
AOEL (Operator/Worker Exposure)	0.0000011 mg/kg bw/day for repeat exposures (corrected for bioavailability 68%)	rabbit teratogenicity study	300 (+ factor 2 to extrapolate from LOAEL

			to NOAEL)
Drinking water limit:	Not applicable		
ARfD (acute reference dose):	Not applicable		-

Acceptable exposure scenarios (including method of calculation)

Professional users	Application scenario: decanting, placing of pellet or grain bait and clean-up Bait size: 200 g Frequency: 79 exposure situations per day Concentration of a.s.: 0.005% (w/w) Acceptable exposure occurs with gloves (% AOEL91). Application scenario: placing of wax block bait and clean-up Bait size: (200 g) calculations based on number (ten) of baits placed per bait site Frequency: 75 exposure situations per day (60 loadings and 15 clean-ups) Concentration of a.s.: 0.005% /w/w) Acceptable exposure occurs with gloves (%AOEL 11.8). Calculations based on the results of an Operator Exposure study.
Non-professional users	Application scenario: placing of pellet or grain bait and clean-up Bait size: 200 g Frequency: 10 exposure situations per day Concentration of a.s.: 0.005% (w/w) Acceptable exposure occurs without gloves (%AOEL 91). Application scenario: placing of wax block bait and clean-up Bait size: (200 g) calculations based on number (ten) of baits per bait site Frequency: 10 exposure situations per day (5 loadings and 5 clean-ups) Concentration of a.s.: 0.005% (w/w) Acceptable exposure occurs when gloves are not worn (% AOEL 10.9). Calculations based on the results of an Operator Exposure study.
Indirect exposure as a result of use	No safe scenario, if estimated according to TNsG and User Guidance

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	S & HS DT_{50}: >1 year (pH 7 and 50°C) DT_{50}: >1 year (pH 9 and 50°C)

	At low pH difenacoum insoluble. <u>A/P</u> DT_{50}: > 1year (pH 4 and 25°C) DT_{50}: >1year (pH 7 and 25°C) DT_{50}: >1year (pH9 and 25°C)
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	<u>S & HS</u> DT_{50}: 3.26 hours at pH 5 DT_{50}: 8.05 hours at pH 7 DT_{50}: 7.32 hours at pH 9 (Data generated in aqueous solution using local natural midsummer sunlight equivalent exposure periods) No degradation products >10% was found. <u>A/P</u> DT_{50}: 38 minutes (summer) DT_{50}: 227 minutes (winter) DT_{50}: 49 minutes (spring) The half-lives have been recalculated in minutes assuming 12 hour day. Data was generated at a latitude 52° North in the early part of spring. Two degradation products >10% were detected, but not identified.
Readily biodegradable (yes/no)	No (All applicants)
Biodegradation in seawater	n.a.
Non-extractable residues	n.a.
Distribution in water / sediment systems (active substance)	n.a. (Difenacoum will probably partition into sewage sludge/sediment due to its high log K_{ow} and poor water solubility.)
Distribution in water / sediment systems (metabolites)	n.a.

Route and rate of degradation in soil

Mineralization (aerobic)	<u>S</u> Radioactivity extractability decreased with time. After 108 days of incubation, radioactivity extracted from soil had decreased to 78.4% for Speyer 2.2, indicating radioactive binding to soil and/or volatilisation (e.g. to CO_2, but formation of CO_2 was not measured in the study). Thus mineralization is less than 22% after 108 days. <u>A/P</u> The calculated half-life in soil is > 300 days based (TGD,

	Table 8, Kp 1.34)
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20 °C, aerobic): 439 days (Speyer 2.2 soil) (S)
	DT_{90lab} (20 °C, aerobic): not determined.
	DT_{50lab} (10 °C, aerobic): not determined.
	DT_{50lab} (20 °C, anaerobic): not determined.
	Degradation in the saturated zone: not determined.
Field studies (state location, range or median with number of measurements)	DT_{50f}: not determined.
	DT_{90f}: not determined.
Anaerobic degradation	n.a.
Soil photolysis	n.a.
Non-extractable residues	Radioactivity extractability decreased with time. After 108 days of incubation, radioactivity extracted from soil had decreased to 78.4% for Speyer 2.2, indicating radioactive binding to soil and/or volatilisation (e.g. to CO_2; the amount of bound residue was not determined by combustion) (S)
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	Non-extractable radioactivity was assumed not to be difenacoum. There were no significant single extractable difenacoum degradates. (S)
Soil accumulation and plateau concentration	n.a.

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	<u>S</u> Log Ka_{oc} estimated to be <1.25 (pH 8.46 mobile phase) by HPLC. Log Ka_{oc} estimated to be 2.08 for trans-difenacoum (pH 7.07) by HPLC. Log Ka_{oc} estimated to be 2.32 for cis-difenacoum (pH 7.07) by HPLC. Log Ka_{oc} estimated to be >5.63 (pH 3.29 mobile phase). by HPLC. Log Ka_{oc} estimated to be >5.63 (pH 4.43 mobile phase). by HPLC. <u>A/P</u> Ka_{oc} 67 (pH 7) by HPLC. K_{oc} value of 1 803 018 calculated by the QSAR equation for 'predominantly hydrophobics' according to the TGD part 3, table 4 (log K_{oc}=0.81 log K_{ow} +0.1) (used in PEC and PNEC calculations). (S, HS, A/P)

Fate and behaviour in air

Direct photolysis in air	n.a.

Quantum yield of direct photolysis	not determined
Photo-oxidative degradation in air	S Model calculation (AopWin 1.91): DT_{50} 2.08 h (12 h, $c_{OH} = 1.5 \times 10^6$ molecules/cm³) DT_{50} 6.24 h (24 h, $c_{OH} = 0.5 \times 10^6$ molecules/cm³) A/P Model calculation (EPIWIN v. 3.12): DT_{50} 2.08 h (OH radicals) DT_{50} 2.015 h (ozone)
Volatilization	S Vapour pressure 6.7 x 10^{-9} Pa Henry's law constant 1.75 x 10^{-6} Pa m^3/mol (based on water solubility of 1.7 mg/l) A/P Vapour pressure < 5 x 10^{-5} Pa at 45 °C (99%), an estimation <0.046 Pa m^3 $mole^{-1}$, an estimation Difencoum is not expected to volatilise to air in significant quantities.

Monitoring data, if available

Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	Not available
Ground water (indicate location and type of study)	Not available
Air (indicate location and type of study)	Not available

Chapter 5: Effects on Non-target Species

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

Species	Timescale	Endpoint	Toxicity
Fish			
Rainbow trout (*Oncorhynchus mykiss)*	96 hours	LC_{50}	0.064 mg/l (S) 0.33 mg/l (A/P)
Invertebrates			
Daphnia magna	48 hours	LC_{50}	0.52 mg/l (S) 0.91 (A/P)
Algae			
Green alga (*Selenastrum capricornutum)*	72 hours	E_rC_{50} NOE_rC	0.80 mg/l (S) 0.25 mg/l (S) 0.51 mg/l (A/P) 0.13 mg/l (A/P)
Microorganisms			

Pseudomonas putida	6 hours	EC_{50}	>2.3 mg/l (S) >999.7 mg/l (A/P)

Effects on earthworms or other soil non-target organisms

Acute toxicity to earthworm (*Eisenia foetida foetida*)……..	>994 mg/kg dry weight (A/P)
Reproductive toxicity to ……	n.a.

Effects on soil micro-organisms

Nitrogen mineralization	n.a.
Carbon mineralization	n.a.

Effects on terrestrial vertebrates

Acute toxicity to mammals	LD_{50} 1.8 mg/kg (male rat) (S) LD_{50} 5-50 mg/kg_{bw} (female rat) (A/P)
Acute toxicity to birds	Bobwhite quail (*Colinus virginianus)* LD_{50}: 56 mg/kg_{bw} (female) (S) Japanese quail (*Coturnix coturnix japonica)* LD_{50}: 133 mg/kg_{bw} (female) (A/P)
Dietary toxicity to birds	Mallard duck (*Anas platyrhynchos)* LC_{50}: 18.9 mg/kg_{food} (S) Japanese quail (*Coturnix coturnix japonica)* LC_{50}: 1.4 mg/kg_{food} (A/P)
Reproductive toxicity to birds	Japanese Quail (*Coturnix coturnix japonica*) NOEC: 0.1 mg/kg_{food} (S, HS) Japanese quail (*Coturnix coturnix japonica*) NOEC: 0.31 mg/$kg_{drinking\ water,}$ NOEL 58 µg/kg_{bw} (A/P)

Effects on honeybees

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

Effects on other beneficial arthropods

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

Bioconcentration

Bioconcentration factor (BCF) - estimated by calculation	BCF_{fish} 35 645 (calculated according to TGD method, Eq. 75, using estimated log K_{ow} value of 7.6) (S, HS, A/P)
	BCF_{fish} 9 010 (calculated according to the EPA EPIWIN BCF estimation program, using log K_{ow} value of 7.6) (S; HS; A/P)
	$BCF_{earthworm}$ 477 729 (calculated according to TGD method, Eq. 82d, using estimated log K_{ow} value of 7.6) (S, HS, A/P)

Chapter 6: Other End Points

None required

Appendix II: List of Intended Uses

Object and/or situation	Member State or Country	Product name	Organisms controlled	Formulation	Concentration	Application
Pest control / In and around buildings Sewers Open areas Waste dumps	All EU Member States	Various	Brown rat (*Rattus norvegicus*) Black rat (*R. rattus)* House mouse (*Mus musculus/domesticus)*	Ready for use baits Pellet bait Block bait Grain bait	50 mg/kg 50 and 75 mg/kg 50 mg/kg	The product is used in the same manner in all of these situations; the bait is manually placed in discrete locations within the infested area, it is not dispersed or broadcast within the environment. The number of bait points employed and the amount of product used is dependant on: the treatment site; the size and severity of the infestation; the user; and the users requirements and needs. For rat control, protected bait points containing up to 200g of product are used, at intervals of up to 10 metres apart. For mouse control, protected bait points containing up to 40g of product are used, at intervals of 1-2 metres apart. An adequate number of baits points are placed in dry locations, protected from the weather and in appropriate positions to help prevent access by non-target animals.

Appendix III: Summary of risk characterisation for users of the representative products

MOE calculations and comparison of exposure with AOEL for users of pellets, grain and wax blocks baits containing 0.005% (50 mg/kg) difenacoum. Repeated dose toxicity NOAEL-value used for the MOE is derived from the LOAEL-value of 0.001 mg/kg bw/day corrected for 68% bioavailability and by factor 2 to extrapolate from LOAEL to NOAEL. Dermal absorption value of 3% is used for pellet and grain baits and the value of 0.047% is used for wax block bait containing 0.005% of difenacoum.

Neosorexa pellet baits or MYOCURATTIN-FCM-Granulat grain baits containing 0.005% (50 mg/kg) difenacoum.

Workplace operation	**PPE**	**Exposure path**	**Body dose mg/kg bw/day**	**Repeated dose toxicity NOAEL = 0.00034 mg/kg/day**	**Repeated dose toxicity AOEL = 0.0000011 mg/kg / day**
				MOE	**%AOEL**
Decanting, placing of pellet or grain bait and clean-up, trained professional	None	Dermal, hands Inhalation	1.0×10^{-5}	34	909
Decanting, placing of pellet or grain bait and clean-up, trained professional	Protective gloves	Dermal, hands Inhalation	1.0×10^{-6}	340	91
Placing of pellet or grain bait and clean-up, non-trained professional	None	Dermal, hands	1.0×10^{-6}	340	91
Placing of pellet or grain bait and clean-up, non-trained professional	Protective gloves	Dermal, hands	1.0×10^{-7}	3400	9.1
Placing of pellet or grain bait and clean-up, amateur	None	Dermal, hands	1.0×10^{-6}	340	91

Roban Wax Block, containing 50 mg/kg (0.005%) difenacoum.

Workplace operation	PPE	Exposure path	Body dose mg/kg bw/day	Repeated dose toxicity NOAEL = 0.00034 mg/kg/day	Repeated dose toxicity AOEL = 0.0000011 mg/kg / day
				MOE	%AOEL
Placing of wax block baits and clean-up, trained professional	None	Dermal, hands Inhalation	1.3×10^{-6}	262	118
Placing of wax block baits and clean-up, trained professional	Protective gloves	Dermal, hands Inhalation	1.3×10^{-7}	2615	11.8
Placing of wax block baits and clean-up, non-trained professional	None	Dermal, hands	1.2×10^{-7}	2833	10.9
Placing of wax block baits and clean-up, non-trained professional	Protective gloves	Dermal, hands	1.2×10^{-8}	28333	1.1
Placing of wax block baits and clean-up, amateur	None	Dermal, hands	1.2×10^{-7}	2833	10.9

Appendix IV: 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 "Yes" in the "Data Protection Claimed" column of the table below. Data protection is claimed under Article 12.1(c) (i) or (ii) and the claims can be found in Doc III-A and Doc III-B. 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.

List of studies of Sorex Limited

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)published	Data Protection Claimed (Yes/No)	Owner
III-A 2.7/01	Axxxx	2000	Difenacoum Technical Specification No. 239, revision 6.00, Issue date 21/09/2000. Gxxxx. Not GLP, unpublished. CONFIDENTIAL	Yes	Sxxxx Lxxxxxx
III-A 2.8/01 III-A 4.1/01	Cxxxx, C and Cxxxx, WB	2000	Difenacoum: Product Chemistry of Difenacoum: Analytical Profile of 5 Batches. Ixxxx, Report No: 17949. GLP, unpublished. [DF-959-0075]. CONFIDENTIAL	Yes	Sxxxx Lxxxxxx
III-A 3.1.1/01 III-A 3.1.2/01 III-A 3.1.3/01 III-A 3.2/01 III-A 3.3.1/01 III-A 3.3.2/01 III-A 3.3.3/01 III-A 3.4.1/01 III-A 3.5/01 III-A 3.7/01 III-A 3.9/01 III-A 7.1.1.1.1/01	Rxxxx, S	1996	Difenacoum: Determination of Physico-chemical Properties. Cxxxx, Report No: 355/7-1014. GLP, unpublished. [DF-959-0018]	Yes	Sxxxx Lxxxxxx
III-A 3.4.2/01 III-A 3.4.3/01 III-A 3.4.4/01	Exxxxx, D	1996	Difenacoum: Determination of Spectroscopic Properties. Cxxxx, Report No: 355/43-1014. GLP, unpublished. [DF-959-0005]	Yes	Sxxxx Lxxxxxx
III-A 3.6/01	Mxxxx, E	2005	Physico-chemical testing with difenacoum: Estimation of dissociation constant and adsorption coefficient. Cxxxx, Report No: 26059. GLP, unpublished. [DF-3.6-0386]	Yes	Sxxxx Lxxxxxx
III-A 3.10/01	Gxxxx, J	2000	Difenacoum: Evaluation of Thermal Properties by Differential Scanning Calorimetry. Cxxxx, Report No: 355/50-D2141. GLP, unpublished. [DF-959-0078]	Yes	Sxxxx Lxxxxxx

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)published	Data Protection Claimed (Yes/No)	Owner
III-A 3.11/01	Yxxxx, S	2005	Physico-Chemical Properties Analysis on Difenacoum, Cxxxx, Report No: GLP 13921R1V1/05 [DF-959-0173]	Yes	Sxxxx Lxxxxxx
III-A 3.15/01 III-A 3.16/01	Rxxxx, S	2005	Assessment of Potential Oxidising and Explosive Properties of Difenacoum, Cxxxx Report No: J13516R1V1/05 [DF-959-0176]	Yes	Sxxxx Lxxxxxx
III-A 3.16/02	Yxxxx, S	2005	Oxidising Properties on a Sample of Difenacoum, Cxxxx, Report No: GLP14238R1V3/05 [DF-959-0364]	Yes	Sxxxx Lxxxxxx
III-A 4.2 (a)/01	Dxxxx, A, Fxxxx, L and Sxxxx, G	2005	Development and Validation of a Method for the Determination of Difenacoum in Soil. Ixxxx, Report No: 25295. GLP, unpublished. [DF-959-0163]	Yes	Sxxxx Lxxxxxx.
III-A 4.2(c)/01	Sxxxx, G et al.	2005	Development and Validation of a Method for the Determination of Difenacoum in Surface Water. Cxxxx, Report Number: 26056 GLP, Not Published	Yes	Sxxxx Lxxxxxx.
III-A 4.2 (c)/02	Sxxxx, G and Dxxxx, J	2005	Development and Validation of a Method for the Determination of Difenacoum in Sediment. Cxxxx, Report Number: 25986 GLP, Not Published	Yes	Sxxxx Lxxxxxx.
III-A 4.2 (d)/01	Dxxxx, A and Mxxxx, G	2002	Development and Validation of a method for determination of difenacoum in rat liver samples. Ixxxx, Report No:21009. GLP, unpublished. [DF-959-0103].	Yes	Sxxxx Lxxxxxx
III-A 4.2(d)/02	Chalermchaikit , T, Felice, LJ and Murphy, MJ	1993	Simultaneous determination of eight anticoagulant rodenticides in blood serum and liver J. Anal. Toxicol. 17, 56-61, Not GLP, Published	No	
III-A 4.3/03	Kxxxx, S	2006	Validation of multi-residue method DFG S19 (L 00.00-34) for the determination of residues of Difenacoum in different plant matrices and meat with LC-MS/MS detection. Exxxx, Report no. HEN-0503V GLP, Not Published	Yes	Xxxxx xxxxxxx & Xxxxxxxx xxx xxxxxxxx
III-A 5.3.1/01 III-A 5.4/01 III-A 6.12.2/01 III-A 6.12.5/02 III-A 6.12.7/02 III-A 6.12.8/01 III-B 5.7/01 III-B 5.8/01	WHO (World Health Organisation publication)	1995	Environmental Health Criteria 175 - Anticoagulant Rodenticides. International Programme on Chemical Safety, pages 22 and 55. Not GLP, published. [DF-959-0142].	No	
III-A 5.4/02	Bxxxx, P	2003	Difenacoum: Review of Mode of Action. Jxxxx. Not GLP, unpublished. [DF-959-0126]	Yes	Sxxxx Lxxxxxx

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II-A 2.3.2	Thijssen, HHW	1995	Warfarin-based rodenticides: Mode of action and mechanism of resistance Pestic. Sci. 43, 73-78, Not GLP, Published	No	
II-A 2.3.3	Pesticides Safety Directorate	1997	Assessment of humaneness of vertebrate control agents. (Food and environment protection act, 1985, part III, control of pesticides regulations 1986, Evaluation of fully approved or provisionally approved products, Issue 171; York YO1 7PX)	No	
II-A 2.3.3	Axxx	1992	Anticoagulant Rodenticide Humaneness Data Overview Part 1 and Part 2. Not GLP, unpublished. GR-959-0075	Yes	Bxxx, Ixxx, Lxxx, Rxxx, Sxxx, and Sxxxx Lxxxxxx.
III-A 5.7/01	Bxxxx, A	2004a	Difenacoum and Resistance Management. Axxxx. Not GLP, unpublished. [DF-959-0150].	Yes	Sxxxx Lxxxxxx
II-A 2.4	Greaves, JH, Shephard, DS and Gil, JE	1982	An investigation of difenacoum resistance in Norway rat populations in Hampshire Ann. Appl. Biol. 100, 581-587, Not GLP, Published	No	
II-A 2.4	Cowan, D, Dunsford, G, Gill, E, Jones, A, Kerins, G, MacNicoll, A and Quy, R	1995	The impact of resistance on the use of second-generation anticoagulants against rats on farms in Southern England Pestic. Sci. 43, 83-93, Not GLP, Published	No	
II-A 2.4	Pelz, H-J, Hänisch, D and Lauenstein, G	1992	Resistenz gegenüber Wirkstoffen aus der Gruppe der Antikoagulantien bei Wanderratten in Nordwestdeutschland Mitt. Biol. Bundesanstalt Land. Forst. 283, 200, Not GLP, Published	No	
II-A 2.4	Pelz, H-J, Hänisch, D and Lauenstein, G	1995	Resistance to anticoagulant rodenticides in Germany and future strategies Pestic. Sci. 43, 61-67, Not GLP, Published	No	
II-A 2.4	Desideri, D, Aldighieri, R, Le Louet, M and Tardieu, A	1979	La résistance murine aux anticoagulants dans le port de Marseille (suite) - état de réponse au difénacoum. Bull. Soc. Pathol. Exotique 72, 278-283, Not GLP, Published	No	
II-A 2.4	Greaves, JH, Shepard, DS and Quy, R	1982	Field trials of second-generation anticoagulants against difenacoum-resistant Norway rat populations. J. Hyg. 89: 295-301.	No	

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II-A 2.4	Greaves, JH and Gullen-Ayres, PB	1988	Genetics of difenacoum resistence in the rat. Suttie, J.W. (ed.): Current Advances in Vitamin K research - A Steenbock Symposium, Elsevier, 389-397, Not GLP, Published	No	
II-A 2.4	Li, T, Chang, C-Y, Jin, D-Y, Lin, P-J, Khvorova, A and Stafford, DW	2004	Identification of the gene for vitamin K epoxide reductase. Nature 427: 541-544.	No	
II-A 2.4	Rost, S, Fregin, A, Ivankevicius, V, Conzelmann, E, Hörtnagel, K, Pelz, H-J, Lappegard, K, Seifred, E, Scharrer, I, Tuddenham, EGD and others	2004	Mutations in VKORC1 cause warfarin resistance in multiple coagulation factor deficiency type 2. Nature 427: 537-541.	No	
II-A 2.4	Pelz, H-J, Rost, S, Hünerberg, M, Fregin,A, Heiberg, A-C, Baert, K, MacNicoll, AD, Prescott, CV, Walker, A-S, Oldenburg, J and Müller, CR	2005	The genetic basis of resistance to anticoagulants in rodents. Genetics, published on May 6, 2005 as 10.1534/genetics.104.040360.	No	
II-A 2.4	Gill, JE, Kerins, GM, Langton, SD and MacNicholl, AD	1993	The development of a blood clotting response test for discriminating between difenacoum-resistant and susceptible Norway (Rattus norvegicus, Berk.) Comp. Biochem. Physiol. 104C, 29-36, Not GLP, Published	No	
II-A 2.4	Quy, RJ, Shepherd, DS and Inglis, IR	1992	Bait avoidance and effectiveness of anticoagulant rodenticides against warfarin- and difenacoum-resistant populations of Norway rats (Rattus norvegicus). Crop Protection 11, 14-20, Not GLP, Published	No	
II-A 2.4	Smith, P, Inglis, IR, Cowan, DP, Kerins, GM and Bull, DS	1994	Symptom-dependent taste aversion induced by an anticoagulant rodenticide in the brown rat (Rattus norvegicus). J. Comp. Psychol. 108, 282-290, Not GLP, Published	No	

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III-A 5.7/02	RRAC	2003	Anticoagulant resistance management strategy for pest management professionals, central and local government and other competent users of rodenticides. CropLife International (Rodenticide Resistance Action Committee) Technical Monograph, Brussels, p. 18 and www.croplife.org	No	
III-A 6.1.1/01	Gxxxx, JR	1995a	Difenacoum: Acute Oral Toxicity Study in the Male Wistar Rat. Cxxxx, Report no: 355/34-1032. GLP, unpublished. [DF-959-0011].	Yes	Sxxxx Lxxxxxx
III-A 6.1.1/02	Gxxxx, JR	1995c	Difenacoum – Acute Oral Toxicity Study in the Rat. Hxxxx, Report No: 355/8-1032. GLP, unpublished. [DF-959-0006].	Yes	Sxxxx Lxxxxxx
III-A 6.1.1/03	Hxxxx, MR	1973a	Acute Oral Toxicity of WBA 8107 to Male Albino Mice. Wxxxx, Report No: RIC0943. Not GLP, unpublished. [C2.1/17].	Yes	Sxxxx Lxxxxxx
III-A 6.1.1/04	Rxxxx, MC	1998	Acute Oral Toxicity (LD_{50}) Tests with Cis- and Trans-isomers and a Racemic Mixture of Difenacoum. Bxxxx, Report No. 3175/2/2/98. GLP, unpublished. [DF-959-0065].	Yes	Sxxxx Lxxxxxx
III-A 6.1.2/01	Gxxxx, JR	1995d	Difenacoum: Acute Dermal Toxicity Study in the Rat. Hxxxx, Report No: 355/9-1032. GLP, unpublished. [DF-959-0007].	Yes	Sxxxx Lxxxxxx
III-A 6.1.3/01	Sxxxx, NM	1996	Difenacoum: Single Dose Inhalation (Head-Only) Toxicity Study in the Rat. Cxxx, Report No: 355/11-1050. GLP, unpublished. [DF-959-0025].	Yes	Sxxxx Lxxxxxx
III-A 6.1.4/01	Gxxxx, JR	1995e	Difenacoum – Skin Irritation Study in the Rabbit. Hxxxx, Report No: 355/010-1032. GLP, unpublished. [DF-959-0008].	Yes	Sxxxx Lxxxxxx
III-A 6.1.4/02	Gxxxx, JR	1995b	Difenacoum: Eye Irritation Study in the Rabbit. Hxxxx, Report No: 355/024-1032. GLP, unpublished. [DF-959-0009].	Yes	Sxxxx Lxxxxxx
III-A 6.1.5/01	Dxxxx, SM	1995	Difenacoum: Skin Sensitisation in the Guinea Pig. Hxxxx, Report No: 355/12-1032. GLP, unpublished. [DF-959-0004].	Yes	Sxxxx Lxxxxxx
III-A 6.1.5/02	Lxxxx, J	2002	Examination of Difenacoum technical in a skin sensitisation test in guinea-pigs according to Magnusson and Kligman (maximisation test). Lxxx, Report No.: 14965/01 GLP, unpublished	Yes	Hxxxxxxx & Sxxxxxx and Sxxxx Lxxxxxx

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III-A 6.2/01	Pxxxx, JC	2002	An investigation into the elimination and tissue distribution of the ^{14}C-labelled stereoisomers of difenacoum following oral administration to rats. Txxxx, Report No: 3175/3/02. GLP, unpublished. [DF-959-0098].	Yes	Sxxxx Lxxxxxx
III-A 6.2/03	Pxxxx, JC	1996	An investigation into the absorption, tissue distribution and elimination of ^{14}C-labelled difenacoum following oral administration to rats. Bxxxx, Report No: 1555/2/3/96. GLP, unpublished. [DF-959-0015].	Yes	Sxxxx Lxxxxxx
III-A 6.2/04	Bxxxx, H	1987	Difenacoum: Elimination from the tissues of rats following administration of a single oral dose. Ixxxx, Report No: CTL/P/1592. GLP, unpublished. [C2.7/01].	Yes	Sxxxx Lxxxxxx
III-A 6.2/05	Bxxxx, PL	2002	Difenacoum: Expert Review of Toxicokinetics. GLP Not Applicable, unpublished. [DF-959-0114].	Yes	Sxxxx Lxxxxxx
III-A 6.4.1/01	Hxxxx, MCE	1994c	Difenacoum: 6 Week Oral Toxicity Study In Dogs. Zxxxx, Report No: TL/L/5738. Not GLP (uncompleted study), unpublished. [CTL/L/5738, SuppSeries].	Yes	Sxxxx Lxxxxxx
III-A 6.4.1/02	Hxxxx, JM	1991	Difenacoum: Oral Toxicity Study In Rats. Ixxxx, Report No: CTL/P/3504. GLP, unpublished. [C2.1/08].	Yes	Sxxxx Lxxxxxx
III-A 6.4.1/03	Lxxxx, J	2003	90-day subchronic toxicity study of Difenacoum technical by repeated oral administration to CD rats Lxxxx, Report No: 14967/01. GLP, unpublished	Yes	Hxxxxxxx & Sxxxxxx and Sxxxx Lxxxxxx
III-A 6.6.1/01	Bxxxx, M	1995	Difenacoum: Reverse Mutation in 5 Histidine requiring strains of Salmonella typhimurium. Hxxxx, Report No: 355/22-1052. GLP, unpublished. [DF-959-0001].	Yes	Sxxxx Lxxxxxx
III-A 6.6.1/02	Cxxxx	1986	Difenacoum - An Evalution in the Salmonella Mutagenicity Assay. Ixxxx, Report No: CTL/P/1448. GLP, unpublished. [C2.6/04].	Yes	Sxxxx Lxxxxxx
III-A 6.6.2/01	Rxxxx, S	1995	Difenacoum: Induction of Chromosome Aberrations in Cultured Human Peripheral Blood Lymphocytes. Cxxxx, Report No: 355/21-1052. GLP, unpublished. [DF-959-0016].	Yes	Sxxxx Lxxxxxx
III-A 6.6.2/02	Wxxxx, J, Hxxxx, CA, Cxxxx, P and Rxxxx, CR	1986	Difenacoum: An In Vitro Cytogenetic Study in Chinese Hamster Lung Fibroblasts. Ixxxx, Report No: CTL/P/1553. GLP, unpublished. [C2.6/02].	Yes	Sxxxx Lxxxxxx

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)published	Data Protection Claimed (Yes/No)	Owner
III-A 6.6.3/01	Cxxxx, J	1995	Difenacoum: Mutation at the Thymidine Kinase (tk) Locus of Mouse Lymphoma L5178Y Cells using the Microtitre Fluctuation Technique. Cxxxx, Report No: 355/16-1052. GLP, unpublished. [DF-959-0003].	Yes	Sxxxx Lxxxxxx
III-A 6.6.4/01	Rxxxx, S	1996	Difenacoum: Induction of Micronuclei in the Bone Marrow of Treated Rats. Cxxxx, Report No: 355/37-1052. GLP, unpublished. [DF-959-0017].	Yes	Sxxxx Lxxxxxx
III-A 6.6.4/02	Sxxxx, T, Rxxxx, CR, Rxxxx, V and Hxxxx, D	1987	Difenacoum: An Evaluation in the Mouse Micronucleus Test. Ixxxx, Report No: CTL/P/1666. GLP, unpublished. [C2.6/03].	Yes	Sxxxx Lxxxxxx
III-A 6.6.5/01	Cxxxx, C	1996	Difenacoum: Measurement of Unscheduled DNA Synthesis in Rat Liver Using an In Vivo/In Vitro Procedure. Cxxxx, Report No: 355/38-1052. GLP, unpublished. [DF-959-0002].	Yes	Sxxxx Lxxxxxx
III-A 6.8.1/01	Hxxxx, MCE	1994a	Difenacoum: Developmental Toxicity Study in the Rat. Zxxxx, Report No: CTL/P/4354. GLP, unpublished. [C2.5/01].	Yes	Sxxxx Lxxxxxx
III-A 6.8.1/02	Hxxxx, MCE	1994b	Difenacoum: Developmental Toxicity Study in the Rabbit. Zxxxx, Report No: CTL/P/4245. GLP, unpublished. [C2.5/02].	Yes	Sxxxx Lxxxxxx
III-A 6.8.1/03	Mxxxx, GJ	2003	Expert Review of Study Report CTL/P/4245 (Difenacoum: Developmental Toxicity Study in the Rabbit, 1994). Cxxxx, dated 15th April 2003. GLP Not Applicable, unpublished. [DF-959-0140].	Yes	Sxxxx Lxxxxxx.
III-A 6.12.1/01 III-A 6.12.3/01 III-A 6.12.6/01	Rxxxx, K	2004	Biological Monitoring of Rodenticide Workers at Pxxxx and Sxxxx. Report prepared for Sxxxx. Not GLP, unpublished. [DF-959-0135]	Yes	Sxxxx Lxxxxxx
III-A 6.12.5/01 III-A 6.12.7/02 III-A 6.12.8/02	Axxxx	2004	The treatment of anticoagulant poisoning: Advice to physicians. Issued jointly by Zxxxx, Sxxxx, Lxxxx, Bxxxx and Bxxxx. Not GLP, unpublished. [Advice to physicians1]	Yes	Sxxxx Lxxxxxx
III-A 6.13/01	Rxxxx, MC	1998	Acute Oral Toxicity (LD_{50}) Tests with Cis- and Trans-isomers and a Racemic Mixture of Difenacoum. Bxxxx, Report No. 3175/2/2/98. GLP, unpublished. [DF-959-0065].	Yes	Sxxxx Lxxxxxx
III-A 6.13/02	Hxxx, MR	1975	The Acute Oral Toxicity of Difenacoum to Female Guinea Pigs. Wxxxx, Report No: RIC0922. [C2.1/11].	Yes	Sxxxx Lxxxxxx

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III-A 6.13/03	Pxxxx, GR	1975	Difenacoum: Acute Oral Toxicity. Ixxxx, Report No: CTL/P/196. Not GLP, unpublished. [C2.1/10].	Yes	Sxxxx Lxxxxxx
III-A 6.13/04	Rxxxx, DB and Rxxxx, NL	1974	The Oral Toxicity of WB 8107 to the Domestic Pig. Hxxxx, Report No: SRX 2/7670. Not GLP, unpublished. [C2.1/07].	Yes	Sxxxx Lxxxxxx
III-A 6.13/05	Hxxxx, MR	1973c	Acute oral toxicity of Wba 8107 to chickens. Wxxxx, Report No: RIC0969. Not GLP, unpublished. [G2.1/05].	Yes	Sxxxx Lxxxxxx
III-A 6.13/06	Hxxxx, MR	1973b	Acute Oral Toxicity of WBA 8107 to Male Albino Rabbits. Wxxxx, Report No: RIC0941. Not GLP, unpublished. [C2.1/15].	Yes	Sxxxx Lxxxxxx
III-A 7.1.1.1.1/02	Lxxxx, C	1992a	Difenacoum: Hydrolysis Study. Hxxxx, Report No: 7031. GLP, unpublished. [F4.1/01].	Yes	Sxxxx Lxxxxxx
III-A 7.1.1.1.2/01	Hxxxx, B, Jxxxx, R and Pxxxx, I	1992	Difenacoum: Photolysis in Buffered Aqueous Solutions. Ixxxx, Report No: 8704. GLP, unpublished. [F4.1/02].	Yes	Sxxxx Lxxxxxx
III-A 7.1.1.2.1/01	Kxxxx, C and Cxxxx, M	2003	Difenacoum – Determination of Ready Biodegradability by the Closed Bottle Test. Ixxxx, Report No: 21948. GLP, unpublished. [DF-959-0123].	Yes	Sxxxx Lxxxxxx
III-A 7.1.2.1.2	Pxxxx, A	2004	Difenacoum: Determination of anaerobic biodegradability, Axxxx, Report No. BL7788/B. GLP, unpublished. [DF-959-0148].	Yes	Sxxxx Lxxxxxx
III-A 7.1.3/01	Hxxxx, A	2002	Difenacoum: Physico-Chemical Testing with Difenacoum: Estimation of Adsorption Coefficient. Ixxxx, Report No: 21677. GLP, unpublished. [DF-959-0117].	Yes	Sxxxx Lxxxxxx
III-A 7.1.3/02	Mxxxx, E	2005	Physico-chemical testing with difenacoum: Estimation of dissociation constant and adsorption coefficient. Cxxxx, Report number 26059. GLP, unpublished. [DF-3.6-0386]	Yes	Sxxxx Lxxxxxx
III-A 7.2.1/01	Lxxxx, C	1992b	(^{14}C)-Difenacoum: A Study of the Degradation in Two Soils. Hxxxx, Report No: 6927. GLP, unpublished. [F3.1/02].	Yes	Sxxxx Lxxxxxx
III-A 7.2.3.2/01	Lxxxx, CJ	1992c	(^{14}C)-Difenacoum: Aged Soil Leaching. Hxxxx, Report No: 7066. GLP, unpublished. [F3.2/02].	Yes	Sxxxx Lxxxxxx
III-A 7.4.1.1/01	Wxxxx, L	1995b	Difenacoum: Acute Toxicity to Oncorhynchus mykiss. Cxxxx, Report Number: 355/17-1018. GLP, unpublished. [DF-959-0030].	Yes	Sxxxx Lxxxxxx
III-A 7.4.1.1/02	Wxxxx, L	1995c	Difenacoum: Acute Toxicity to Lepomis macrochirus. Cxxxx, Report Number: 355/23-1018. GLP, unpublished. [DF-959-0033].	Yes	Sxxxx Lxxxxxx

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III-A 7.4.1.2/01	Wxxxx, L	1995a	Difenacoum: Acute Toxicity to Daphnia magna. Cxxxx, Report no: 355/18-1018. GLP, unpublished. [DF-959-0031].	Yes	Sxxxx Lxxxxxx
III-A 7.4.1.2/02	Kxxxx, S et al.	1991	Difenacoum: Acute Toxicity to Daphnia magna. Ixxxx, Report no:BL4314/B. GLP, unpublished. [G6.1/01D].	Yes	Sxxxx Lxxxxxx
III-A 7.4.1.3/01	Wxxxx, L	1995d	Difenacoum: Inhibition of growth to the alga Selenastrum capricornutum. Cxxxx, Report Number : 355/19-1018. GLP, unpublished. [DF-959-0032].	Yes	Sxxxx Lxxxxxx
III-A 7.4.1.3/02	Sxxxx, D	1991	Difenacoum: Toxicity to the green alga Selenastrum capricornutum. Ixxxx, Report Number : BL4307/B. GLP, unpublished. [G8.1/01].	Yes	Sxxxx Lxxxxxx
III-A 7.4.1.4/01	Mxxxx, J and Txxxx, J	1989	Difenacoum: Determination of the toxicity to Pseudomonas putida. Ixxxx, Report No : BL/B/3466. GLP, unpublished. [G7.1/01].	Yes	Sxxxx Lxxxxxx
III-A 7.4.1.4/02	Dxxxx, M	2001	Activated Sludge Respiration Inhibition Test with DIFENACOUM (Contact Time: 30 Minutes). Nxxxx, Report No. 328837. GLP, unpublished. [DF-959-0096].	Yes	Sxxxx Lxxxxxx
III-A 7.5.3.1.1/01	Nxxxx, S	1997	Difenacoum: Acute Oral Toxicity to Mallard Duck. Cxxxx, Report No: 355/39-1007. GLP, unpublished. [DF-959-0042].	Yes	Sxxxx Lxxxxxx
III-A 7.5.3.1.1/02	Rxxxx, D, Rxxxx, N and Fxxxx C	1980a	The Acute Oral Toxicity (LD_{50}) of difenacoum to the Bobwhite Quail. Hxxxx, Report No: ICI 309 WL/8076. GLP, unpublished. [G2.1/03].	Yes	Sxxxx Lxxxxxx
III-A 7.5.3.1.2/01	Rxxxx, D, Rxxxx, N and Fxxxx, C	1980b	The subacute dietary toxicity (LC_{50}) of difenacoum to the Mallard Duck. Hxxxx, Report No: ICI 304/791198. Not GLP, unpublished. [G2.1/02].	Yes	Sxxxx Lxxxxxx
III-A 7.5.3.1.2/02	Nxxxx, S	2000c	Difenacoum: Acute Dietary Toxicity to Bobwhite Quail. Cxxxx, Report No: 355/41-1007. GLP, unpublished. [DF-959-0043].	Yes	Sxxxx Lxxxxxx
III-A 7.5.3.1.2/03	Nxxxx, S	2000a	Difenacoum: Acute Dietary Toxicity to Mallard Duck. Cxxxx, Report No: 355/40-D1141. GLP, unpublished. [DF-959-0077].	Yes	Sxxxx Lxxxxxx
III-A 7.5.3.1.2/04	Nxxxx, S	2000b	Difenacoum: Acute Dietary Toxicity to Ring-necked Pheasants. Cxxxx, Report No: 355/42-D1142. GLP, unpublished [DF-959-0082].	Yes	Sxxxx Lxxxxxx
III-A 7.5.3.1.2/05	Rxxxx, D, Rxxxx, N and Fxxxx, C	1980c	The subacute dietary toxicity (LC_{50}) of difenacoum to the Bobwhite Quail. Hxxxx, Report No: ICI 305/791197. Not GLP, unpublished. [G2.1/01].	Yes	Sxxxx Lxxxxxx

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III-A 7.5.3.1.3/01	Bxxxx, J	2005	Avian reproduction study with Difenacoum in the Japanese quail (*Coturnix coturnix japonica*). Gxxxx, Report no. 04012 GLP, Not Published	Yes	Sxxxx Lxxxxxx
III-A 7.5.6/01 II-C 2.4.3.3	Mendenhall, VM and Pank, LF	1980	Secondary Poisoning of owls by anticoagulant rodenticides. The Wildlife Society Bulletin, 8, 4, 311-315. Not GLP, published. [DF-959-0145].	No	
III-A 7.5.6/02 II-C 2.4.3.3	Gray, A, Eadsforth, CV, Dutton, AJ and Vaughan, JA	1992	Toxicity of second generation rodenticides to Barn Owls. Proceedings Brighton Crop Protection Conference, 781-786. Not GLP, published. [DF-959-0144]	No	
III-A 7.5.6/03 II-C 2.4.3.3	Newton, I, Wyllie, I and Freestone, P	1990	Rodenticides in British Barn Owls. Environmental Pollution, 68, 101–117. Not GLP, published. [DF-959-0143].	No	
III-A 7.6/01	Bxxxx, A	2004b	Expert Review of Literature on the Ecotoxicology of Difenacoum and Wildlife in the European Union. Axxxx. Not GLP, unpublished. [DF-959-0147].	Yes	Sxxxx Lxxxxxx
III-A 8/01	Axxxx	2002	Difenacoum Technical Material, Safety Data Sheet, version DIFE2400 1.00 English. Sxxxx. Not GLP, published.	Yes	Sxxxx Lxxxxxx
III-B 2.2/01	Axxxx	2002	Difenacoum Technical Material (Component 1) Safety Data Sheet. Sxxxx. Not GLP, published.	Yes	Sxxxx Lxxxxxx
III-B 2.2/02	Axxxx	2002	Component 2 Safety Data Sheet. Cxxxx. Not GLP, published. CONFIDENTIAL	No	
III-B 2/2/03	Axxxx	2003	Component 3 Safety Data Sheet. Pxxxx. Not GLP, published. CONFIDENTIAL	No	
III-B 2.2/04	Axxxx	2003	Component 4 Safety Data Sheet. BASF. Not GLP, published. CONFIDENTIAL	No	
III-B 2.2/05	Axxxx	2001	Component 5 Safety Data Sheet. Mxxxx. Not GLP, published. CONFIDENTIAL	No	
III-B 2.2/06	Axxxx	2002	Component 6 Safety Data Sheet. Cxxxx. Not GLP, published. CONFIDENTIAL	No	
III-B 2.2/07	Axxxx	2001	Component 7 Safety Data Sheet. Lxxxx. Not GLP, published. CONFIDENTIAL	No	
III-B 2.2/08	Axxxx	2003	Component 8 Safety Data Sheet. Cxxxxx. Not GLP, published. CONFIDENTIAL	No	
III-B 2.2/09	Axxxx	2003	Component 9 Safety Data Sheet. Vxxxx. Not GLP, published. CONFIDENTIAL	No	
III-B 2.2/10	Axxxx	2000	Component 10 Safety Data Sheet. Hxxxx. Not GLP, published. CONFIDENTIAL	No	

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III-B 2.3/01 III-B 3/01	Txxxx, A and Txxxx, T	1998	Neosorexa Pellets: Physico-Chemical Testing with Neosorexa Pellets. Ixxxx, Report Number: 16143. GLP, unpublished. [NP-959-0057].	Yes	Sxxxx Lxxxxxx
III-B 3.7/01	Hxxxx, CS	1998	Choice feeding (palatability) tests on Neosorexa Pellet bait, fresh and post 24 month stored at ambient conditions, against male Wistar rats. Sxxxx, report number: LR020/98. Not GLP, unpublished.	Yes	Sxxxx Lxxxxxx
III-B 3.7/02	Hxxxx, CS	1998	Choice feeding (palatability) tests on Neosorexa Pellet bait, fresh and post 24 month stored at ambient conditions against male BKW mice. Sxxxx, Report number: LR021/98. Not GLP, unpublished.	Yes	Sxxxx Lxxxxxx
III-B 3.7/03	Bxxxx, ML	2003	Neosorexa Pellets: Evaluation of the two-year ambient temperature storage stability. Cxxxx, Report number: 355/54-D2149. GLP, unpublished. [NP-959-0125].	Yes	Sxxxx Lxxxxxx
III-B 4.1/01	Axxxx	1998	Sorex method 102: The determination of active substances within rodenticidal baits. Sxxxx. Not GLP, unpublished.	Yes	Sxxxx Lxxxxxx
III-B 5.4/01	Anon	2001	British Pest Control Association, 2001. Guidelines for the safe use of anticoagulant rodenticides by professional users. Not GLP, published. [PT-958-1225].	No	
III-B 5.8/02	Bxxxx, P	2003	Difenacoum: Review of Mode of Action. Jxxxx. Not GLP, unpublished. [DF-959-0126].	Yes	Sxxxx Lxxxxxx
III-B 5.10.2/01	Rxxxx, C	1997	Three day no choice feeding tests on Neosorexa Pellet bait against male and female Rattus norvegicus, Wistar strain. Sxxxx, Report number: LR005/97. Not GLP, unpublished.	Yes	Sxxxx Lxxxxxx
III-B 5.10.2/02	Rxxxx, C	1997	Three day no choice feeding tests on Neosorexa Pellet bait against male and female Mus domesticus, BKW strain. Sxxxx, Report number: LR006/97. Not GLP, unpublished.	Yes	Sxxxx Lxxxxxx
III-B 5.10.2/03	Rxxxx, C	1997	Three day no choice feeding tests on Neosorexa Pellet bait against male and female Mus domesticus, Cambridge Cream (warfarin resistant) strain. Sxxxx, Report number: LR010/97. Not GLP, unpublished.	Yes	Sxxxx Lxxxxxx

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)published	Data Protection Claimed (Yes/No)	Owner
III-B 5.10.2/04	Rxxxx, C	1997	Three day no choice feeding tests on Neosorexa Pellet bait against male and female Rattus norvegicus, Welsh (warfarin resistant) strain. Sxxxx, Report number: LR011/97 (unpublished).	Yes	Sxxxx Lxxxxxx
III-B 5.10.2/05	Rxxxx, C	1997	Choice feeding (palatability) tests on Neosorexa Pellet bait against male and female Rattus norvegicus, Wistar strain. Sxxxx, Report number: LR012/97. Not GLP, unpublished.	Yes	Sxxxx Lxxxxxx
III-B 5.10.2/06	Rxxxx, C	1997	Choice feeding (palatability) tests on Neosorexa Pellet bait against male and female Mus domesticus, BKW strain. Sxxxx, Report number: LR013/97. Not GLP, unpublished.	Yes	Sxxxx Lxxxxxx
III-B 5.10.2/07	Bxxxx, E	1997	A trial of Neosorexa Pellets for the control of the Norway rat, Rattus norvegicus. Exxxx. Not GLP, unpublished. [NP-RT-009].	Yes	Sxxxx Lxxxxxx
III-B 5.10.2/08	Bxxxx, E	1997	A trial of Neosorexa Pellets for the control of the Norway rat, Rattus norvegicus. Exxxx. Not GLP, unpublished. [NP-RT-012].	Yes	Sxxxx Lxxxxxx
III-B 5.10.2/09	Bxxxx, E	1997	A trial of Neosorexa Pellets for the control of the House mouse, Mus domesticus, at Gronwen (commercial site), Shropshire. Exxxx. Not GLP, unpublished. [NP-MC-018].	Yes	Sxxxx Lxxxxxx
III-B 5.10.2/10	Bxxxx, E	1997	A trial of Neosorexa Pellets for the control of the House mouse, Mus domesticus, at Gronwen (domestic site), Shropshire. Exxxx. Not GLP, unpublished. [NP-MC-019].	Yes	Sxxxx Lxxxxxx
III-B 5.10.x	Txxxx, R	1998	Mould growth evaluation on Sorex difenacoum pellets and Sorex blank pellets. Sxxxx, Report number LR014/98. Not GLP, unpublished.	Yes	Sxxxx Lxxxxxx
III-B 5.11.2/01	Bxxxx, A	2004	Difenacoum and Resistance Management. Axxxx. Not GLP, unpublished. [DF-959-0150].	Yes	Sxxxx Lxxxxxx
III-B 6.1.1/01	Rxxxx, CS	1997	Bait LD50 Feeding Test on Neosorexa Pellet Bait against male and female Rattus norvegicus, Wistar strain. Sxxxx, Report number: LR014/97. Not GLP, unpublished.	Yes	Sxxxx Lxxxxxx
III-B 6.1.2/01	Dxxxx, E	1998	Neosorexa Pellets: Acute Dermal Toxicity (Limit) Test in Rats. Ixxxx, Report Number: 16434. GLP, unpublished. [NP-959-0050].	Yes	Sxxxx Lxxxxxx

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)published	Data Protection Claimed (Yes/No)	Owner
III-B 6.2/01	Dxxxx, E	1998	Neosorexa Pellets: Acute Dermal Irritation Test in Rabbits. Ixxxx, Report Number: 16194. GLP, unpublished. [NP-959-0058].	Yes	Sxxxx Lxxxxxx
III-B 6.2/02	Dxxxx, E	1998	Neosorexa Pellets: Acute Eye Irritation Test in Rabbits. Ixxxx, Report Number: 16195. GLP, unpublished. [NP-959-0059].	Yes	Sxxxx Lxxxxxx
III-B 6.3/01	Dxxxx, E	1998	Neosorexa Pellets: Buehler Test in Guinea Pigs for Delayed Skin Sensitisation Potential. Ixxxx, Report Number: 16435. GLP, unpublished. [NP-959-0047].	Yes	Sxxxx Lxxxxxx
III-B 6.4/01	Daxxxx, DJ	2005	50ppmDifenacoum Pellet Bait: *In vitro* absorption of difenacoum through human epidermis. Cxxxx, Report No. CTL/JV1861. GLP, unpublished.	Yes	Sxxxx Lxxxxxx
III-B 6.4/02	Wxxxx, RJ and Jxxxx, L	2006	0.5% Difenacoum liquid master: *in vitro* absorption of difenacoum through human epidermis. Cxxxx, Report No. CTL/JV1915. GLP, unpublished. [DL-6.4-0416]	Yes	Sxxxx Lxxxxxx
III-B 6.6/01	Cxxxx, JG and Sxxxx, PJ	2004	Study to determine potential exposure to operators during simulated use of anticoagulant rodenticide baits. Sxxxx, Study No SYN/1302, January 2003. GLP, unpublished. [DF-959-0153].	Yes	Sxxxx Lxxxxxx
III-B 6.6/02	Vxxxx, D and Sxxxx, T	2006	Estimation of the frequency of dermal exposure during the occupational use of rodenticides. Report of EBRC Consulting under contact to CEFIC Rodenticide Working Group	Yes	Sxxxx Lxxxxxx
II-B 3.3.1 II-C 2	Larsen, J	2003	Emission scenario document for biocides used as rodenticides. EUBEES.	No	
II-B 3.3.1 II-C 2	Anon	2003	Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances, Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. Part II.	No	
III-B 7.1/01	Sxxxx, J and Axxxx, D	1982	Difenacoum: Leaching of Formulated Material in Soil Columns. Ixxxx, Report No: RJ 0266B. Not GLP, unpublished. [F3.2/03]	Yes	Sxxxx Lxxxxxx
III-B 7.6.1/02 III-B 7.8.7.2/01	Nxxxx, S and Bxxxx, W	2004	Neosorexa Pellets: food preference (choice) study in the Mallard duck. Cxxxx, Report Number 0355/057-D6154. GLP, unpublished.[NP-959-0134].	Yes	Sxxxx Lxxxxxx

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)published	Data Protection Claimed (Yes/No)	Owner
III-B 7.8.1/04	Rxxxx, M	1998	Acute oral toxicity (LD50) tests with *cis*- and *trans*- isomers and a racemic mixture of difenacoum. Bxxxx, Report No. 3175/2/2/98. Not GLP, unpublished. [DF-959-0065].	Yes	Sxxxx Lxxxxxx
III-B 8/01	Axxxx	2003	Neosorexa Pellets Safety Data Sheet. Sxxxx. Not GLP, published.	Yes	Sxxxx Lxxxxxx
II-C 2.4.2.3	Bxxxx, A	2004	Expert review of literature on the ecotoxicology of difenacoum and wildlife in the European Union. Axxxx.	Yes	Sxxxx Lxxxxxx
II-C 2.4.3.3	Atterby, H, Kerins, GM and MacNicoll, AD	2005	Whole-carcass residues of the rodenticide difenacoum in anticoagulant-resistant and –susceptible rat strains (*Rattus norvegicus*). Environmental Toxicology and Chemistry 24: 318-323.	No	
II-C 2.4.3.4	Newton, I, Wyllie, I and Dale, L	1997	Mortality causes in British Barn Owls (*Tyto alba*), based on 1,101 carcasses examined during 1963-1996. In Duncan JR, Johnson DH, Nicholls TH editors. Biology and conservation of owls in the northern hemisphere, Winnipeg, Canada. United States Department of Agriculture, p. 299-307.	No	
II-C 2.4.3.4	Shore, RF, Birks JDS, Afsar, A, Wienburg, CL and Kitchener, AC	2003	Spatial and temporal analysis of second-generation anticoagulant rodenticides in polecats (*Mustela putorius*) from their range in Britain, 1992-1999. Environmental Pollution 122: 183-193.	No	
II-C 2.4.3.4	Birks, JDS	1998	Secondary rodenticide poisoning risk arising from winter farmyard use by the European Polecat *Mustela putorius*. Biological Conservation 85: 233-240.	No	
II-C 2.4.3.4	Fletcher, MR, Hunter, K, Barnett, EA and Sharp, EA	1999	Pesticide Poisoning of Animals 1998: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	No	
II-C 2.4.3.4	Fletcher, MR, Hunter, K, Barnett, EA and Sharp, EA	2000	Pesticide Poisoning of Animals 1999: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	No	
II-C 2.4.3.4	Barnett, EA, Fletche, MR, Hunter, K and Sharp, EA	2002a	Pesticide Poisoning of Animals 2000: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	No	

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II-C 2.4.3.4	Barnett, EA, Fletcher, MR, Hunter, K and Sharp, EA	2002b	Pesticide Poisoning of Animals 2001: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	No	
II-C 2.4.3.4	Barnett, EA, Fletcher, MR, Hunter, K and Sharp, EA	2003	Pesticide Poisoning of Animals 2002: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	No	
II-C 2.4.3.4	Barnett, EA, Fletcher, MR, Hunter, K and Sharp, EA	2004	Pesticide Poisoning of Animals 2003: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	No	
II-C 2.4.3.5	BirdLife International	2004	Birds in Europe: population estimates, trends, and conservation status. - BirdLife Conservation Series No. 12, Cambridge, UK.	No	
II-C 2.4.3.6	Brakes, CR and Smith, RH	2005	Exposure of non-target small mammals to rodenticides: short-tem effects, recovery and implications for secondary poisoning. Journal of Applied Ecology 42: 118-128.	No	

List of studies of the Activa/Pelgar Brodifacoum and Difenacoum Task Force

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP /(Un)Unpublished	Data Protection Claimed (Yes/No)	Owner
A3.1.1 A3.1.2(1)	Drake RM	2003	Determination of the Melting Point and Boiling Point of Difenacoum Technical Chemex Environmental International Ltd., Report No. ENV5799/120139. GLP, Unpublished	Y	PelGar and Activa
A3.1.2(2)	Drake RM	2005	Determination of the Thermal Stability and Breakdown Products of Difenacoum Chemex Environmental International Ltd., Report No. ENV7063/120139. GLP, Unpublished	Y	PelGar and Activa
A3.1.3	Garofani S	2001	Difenacoum – Determination of the Relative Density ChemService S.r.l., Report No. CH-152/2000 GLP, Unpublished	Y	Activa
A3.2	Fabbrini R	1997	Difenacoum - Determination of the Vapour Pressure ChemService S.p.A., Report No. CH-14/96-C-DIF GLP, Unpublished	Y	PelGar and Activa
A3.2.1	Worthington M	2006	Calculation of Henry's Law Constant SafePharm Laboratories Unpublished	N	PelGar and Activa
A3.3.1 A3.3.2 A3.3.3	Tomlin CDS	2003	The Pesticide Manual 13th ed., Alton, UK: BCPC Publications Published	N	Public Domain
A3.4.1 A3.4.2 A3.4.3 A3.4.4	Garofani S	2001	Difenacoum – UV/Vis, MS, IR and NMR Spectra ChemService S.r.l., Report No. CH-132/2001 GLP, Unpublished	Y	PelGar
A3.5	Woolley SM and Mullee DM	2005	Difenacoum – Determination of Water Solubility SafePharm Laboratories Ltd., Report No. 1558/011 GLP, Unpublished	Y	PelGar and Activa
A3.6	SafePharm Laboratories	2004	ACD/I- Lab Web Service (ACD/pKa 8.02) QSAR SafePharm Laboratories Ltd. Unpublished	N	Public domain
A3.7	Staniland J	2005	The Solubility of Difenacoum in Organic Solvents Chemex Environmental International Ltd., Report No. ENV7059/120139 GLP, Unpublished	Y	PelGar and Activa

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP /(Un)Unpublished	Data Protection Claimed (Yes/No)	Owner
A3.9 (1)	Fabbrini R	1997	Difenacoum – Determination of the Partition Coefficient ChemService S.p.A., Report No. CH-14/96-B-DIF GLP, Unpublished	Y	Activa
A3.9 (2)	Worthington M	2006	Calculation of Partition-coefficient SafePharm Laboratories Ltd. Unpublished	N	PelGar and Activa
A3.10	Drake RM	2005	Determination of the Thermal Stability and Breakdown Products of Difenacoum Chemex Environmental International Ltd., Report No. ENV7063/120139 GLP, Unpublished	Y	PelGar and Activa
A3.11 (1)	Garofani S	2001	Difenacoum – Determination of the Flammability ChemService S.r.l., Report No. CH-153/2000 GLP, Unpublished	Y	PelGar and Activa
A3.11 (2)	Garofani S	2001	Difenacoum – Determination of the Self-Ignition Temperature for Solids. ChemService, Report No. CH-155/2000 GLP, Unpublished	Y	PelGar and Activa
A3.13	Sacker DJ	2005	Determination of the Surface Tension of Difenacoum Chemex Environmental International Ltd., Report No. ENV7163/120139 GLP, Unpublished	Y	PelGar and Activa
A3.15	Garofani S	2001	Difenacoum – Determination of the Explosive Properties ChemService S.r.l., Report No. CH-154/2000 GLP, Unpublished	Y	PelGar and Activa
A3.16 (1)	Garofani S	2001	Difenacoum – Determination of the Oxidizing Properties ChemService S.r.l., Report No. CH-156/2000 GLP, Unpublished	Y	PelGar and Activa
A3.16 (2)	Garofani S	2006	Difenacoum Technical – Determination of the Oxidizing Properties ChemService S.r.l., Report No. CH-267/2006 GLP, Unpublished	Y	PelGar and Activa
A4.1 (2)	Londyn IM	2001	Difenacoum – Five-batch Analysis Pliva-Lachema a.s, Report No. 01/07/002/PLG. GLP, Unpublished	Y	PelGar
A4.2 (a)	Morlacchini M	2005	Residues Determination of Brodifacoum, Difenacoum and Bromadiolone in soil, Cerzoo, Report CZ/05/002/Activa/Soil. GLP, Unpublished	Y	PelGar and Activa

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP /(Un)Unpublished	Data Protection Claimed (Yes/No)	Owner
A4.2 (c)	Martinez MP	2005	Difenacoum Technical: Validation of the Analytical Method for the Determination of the Residues in Drinking, Ground and Surface Waters ChemService S.r.l., Report No. CH-288/2005. GLP, Unpublished	Y	PelGar and Activa
A4.2 (d)	Papa P and Rocchi L	2001	Methods of Analysis of the Rodenticide Residues in Human and Animal Body Fluids and Tissues: Difenacoum Analytical Clinical Toxicology Laboratory. GLP, Unpublished	Y	PelGar and Activa
A4.3	Turnbull G	2005	Validation of Analytical Methodology to Determine Rodenticides in Food Matrices Central Science Laboratory, Report No. PGD-180. GLP, Unpublished	Y	CEFIC/EBPF Rodenticides data development group
A5	Brunton CFA, Macdonald DW and Buckle AP	1993	Behavioural Resistance Towards Poison Baits in Brown Rats Behavioural Processes Published	N	Public Domain
A5	Greaves JH, Shepherd DS and Quy R	1982a	Field trials of Second-Generation Anticoagulants Against Difenacoum-Resistant Norway Rat Populations Journal of Hygiene, 89, 295-301. Published	N	Public Domain
A5	Greaves JH and Cullen-Ayres PB	1988	Genetics of Difenacoum Resistance in the Rat In: Suttie JW (ed.) Current Advances in Vitamin K Research. Elsevier, Amsterdam, pp. 389-397. Published	N	Public Domain
A5	Humphries RE, Meeham AP and Sibly RM	1992	The Characteristics and History of Behavioural Resistance in Inner-city House Mice in the UK In: Borrecco JE and Marsh RE (eds.) 15th Vertebrate Pest Conference. University of California, Davis, pp. 161-164. Published	N	Public Domain
A5	Lund M	1984	Resistance to the Second-Generation Anticoagulant Rodenticides In: Clark DO (ed.) 11th Vertebrate Pest Conference. University of California, Davis pp 89-94. Published	N	Public Domain
A5	MacNicoll AD and Gill JE	1987	The occurrence and significance of rodenticide resistance in the UK In: Lawson, T. J. (ed.) Stored Products Pest Control. British Crop Protection Council Monograph No. 37. BCPC Publications, Thorton Heath, UK, pp. 89-95. Published	N	Public Domain

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A5	Misenheimer TM and Suttie JW	1990	Warfarin Resistance in a Chicago Strain of Rats Biochemical Pharmacology, 40 (9), 2079-2084. Published	N	Public Domain
A5	Quy RJ, Shepherd DS and Inglis IR	1992a	Bait Avoidance and Effectiveness of Anticoagulant Rodenticides Against Warfarin- and Difenacoum-Resistant Populations of Norway Rats Crop Protection, 11, 14-20. Published	N	Public Domain
A5	Quy RJ, Cowan DP, Haynes P, Inglis IR and Swinney T	1992b	The Influence of Stored Food on the Effectiveness of Farm Rat Control British Crop Protection Conference, Pests and Diseases, 4A-3, pp. 291-300. Published	N	Public Domain
A5	Thijssen HHW	1988	Warfarin Inhibition of Vitamin K Epoxide Reductase of Scottish Resistant Rats is Reversible. Published In: Suttie JW (ed.) Current Advances in Vitamin K Research, Elsevier, Amsterdam, pp 429-434. Published	N	Public Domain
A5	RRAC (Rodenticide Resistance Action Committee)	2003	Technical Monograph 2003 - Anticoagulant Resistant Management Strategy For Pest Management Professionals Croplife International Ltd. Published	N	Public Domain
II-A 2.3.3	Cowan, D.; et al.	1995	The impact of resistance on the use of second-generation anticoagulants against rats on farms in Southern England Pestic. Sci. 43, 83-93. Published	N	Public Domain
II-A 2.3.3	Desideri, D, Aldighieri, R, Le Louet, M and Tardieu, A	1979	La résistance murine aux anticoagulants dans le port de Marseille (suite) - état de réponse au difénacoum. Bull. Soc. Pathol. Exotique 72, 278-283. Published	N	Public Domain
II-A 2.3.3	Gill, JE, Kerins, GM, Langton, SD and MacNicholl, AD	1993	The development of a blood clotting response test for discriminating between difenacoum-resistant and susceptible Norway (Rattus norvegicus, Berk.) Comp. Biochem. Physiol. 104C, 29-36. Published	N	Public Domain
II-A 2.3.3	Greaves, JH, Shephard, DS and Gil, JE	1982b	An investigation of difenacoum resistance in Norway rat populations in Hampshire Ann. Appl. Biol. 100, 581-587. Published	N	Public Domain
II-A 2.3.3	Li, T, Chang, C-Y, Jin, D-Y, Lin, P-J, Khvorova, A and Stafford, DW	2004	Identification of the gene for vitamin K epoxide reductase. Nature 427: 541-544. Published	N	Public Domain

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP /(Un)Unpublished	Data Protection Claimed (Yes/No)	Owner
II-A 2.3.3	MacNicoll, A.D.; Gill, J.E.	1993	Vitamin K3 in feedstuffs: antidotal effects in captive anticoagulant-resistant rats and mice J. Wildl. Manage. 57, 835-841. Published	N	Public Domain
II-A 2.3.3	Pelz, H-J, Hänisch, D and Lauenstein, G	1995	Resistance to anticoagulant rodenticides in Germany and future strategies Pestic. Sci. 43, 61-67. Published	N	Public Domain
II-A 2.3.3	Pelz, H-J, Rost, S, Hünerberg, M, Fregin,A, Heiberg, A-C, Baert, K, MacNicoll, AD, Prescott, CV, Walker, A-S, Oldenburg, J and Müller, CR	2005	The genetic basis of resistance to anticoagulants in rodents. Genetics, published on May 6, 2005 as 10.1534/genetics.104.040360. Published	N	Public Domain
II-A 2.3.3	Rost, S, Fregin, A, Ivankevicius, V, Conzelmann, E, Hörtnagel, K, Pelz, H-J, Lappegard, K, Seifred, E, Scharrer, I, Tuddenham, EGD and others	2004	Mutations in VKORC1 cause warfarin resistance in multiple coagulation factor deficiency type 2. Nature 427: 537-541. Published	N	Public Domain
II-A 2.3.3	Rowe, F.P.; Swinney, T.	1988	The efficacy of two permanent poison-baiting measures against mus domesticus living in farm buildings in the UK EPPO Bull. 18, 229-235. Published	N	Public Domain
II-A 2.3.3	Smith, P, Inglis, IR, Cowan, DP, Kerins, GM and Bull, DS	1994	Symptom-dependent taste aversion induced by an anticoagulant rodenticide in the brown rat (Rattus norvegicus). J. Comp. Psychol. 108, 282-290. Published	N	Public Domain
II-A 2.3.3	Thijssen, HHW	1995	Warfarin-based rodenticides: Mode of action and mechanism of resistance Pestic. Sci. 43, 73-78. Published	N	Public Domain
A6.1.1	xxxxxxx	2004	Acute Oral Toxicity Study (Acute Toxic Class Method) of Test Item Difenacoum Technical in Rats xxxxxxx Report No. 04/904-001P. GLP, Unpublished	Y	PelGar and Activa
A6.1.2	xxxxxxx	2004	Acute Dermal Toxicity Study of Test Item Difenacoum Technical in Rats xxxxxxx Report No. 04/904-002P. GLP, Unpublished	Y	PelGar and Activa

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A6.1.3	xxxxxxx	1995	Difenacoum – 4-Hour Acute Inhalation Toxicity Study to the Rat, xxxxxxx Report No MLS/9825. GLP, Unpublished	Y	PelGar
A6.1.4 (1)	xxxxxxx	2004	Acute Skin Irritation Study of the Test Item Difenacoum Technical in Rabbits, xxxxxxx Report Number 04/904-006N. GLP, Unpublished	Y	PelGar and Activa
A6.1.4 (2)	xxxxxxx	2004	Acute Eye Irritation Study of Test Item Difenacoum Technical in rabbits xxxxxxx Report No. 04/904-005N. GLP, Unpublished	Y	PelGar and Activa
A6.1.5 (1)	xxxxxxx	1996	Skin Sensitization Test in Guinea Pigs xxxxxxx, Report No. 14302 TSG. GLP, Unpublished	Y	PelGar and Activa
A6.1.5 (2)	xxxxxxx	1995	Difenacoum - Skin Sensitisation to the Guinea Pig of a 2.5 % Concentrate xxxxxxx Report No. MLS/10009. GLP, Unpublished	Y	PelGar
A6.2 (1)	xxxxxxx	2006	Difenacoum - Metabolism in Rats xxxxxxx Report No. PLG0005. GLP, Unpublished	Y	PelGar and Activa
A6.4.1	xxxxxxx	1995	Difenacoum – 90-day Feeding Study in the Rat xxxxxxx Report No. MLS/10016. GLP, Unpublished	Y	PelGar and Activa
A6.6.1	xxxxxxx	2002	Difenacoum – Reverse Mutation Assay "Ames Test", Using Salmonella typhimurium xxxxxxx Report No. 1558/005. GLP, Unpublished	Y	PelGar and Activa
A6.6.2	xxxxxxx	2002	Difenacoum – Chromosome Aberration Test In Human Lymphocytes in vitro xxxxxxx Report No. 1558/001. GLP, Unpublished	Y	PelGar and Activa
A6.6.3	xxxxxxx	2004	Difenacoum – L5178Y TK+/- Mouse Lymphoma Assay xxxxxxx Report No.1558/002. GLP, Unpublished	Y	PelGar and Activa
A6.6.4	xxxxxxx	1995	Difenacoum – An Evaluation in the Mouse Micronucleus Test xxxxxxx Report No. MLS/10029. GLP, Unpublished	Y	PelGar and Activa

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A6.6.5	xxxxxxx	1995	Difenacoum – Assessment for the Induction of Unscheduled DNA Synthesis in Rat Hepatocytes xxxxxxx Report No. MLS/10021. GLP, Unpublished	Y	PelGar and Activa
A6.8.1 (1)	xxxxxxx	1995	Difenacoum – Development Toxicity to the Rat xxxxxxx Report No. MLS/10013. GLP, Unpublished	Y	PelGar and Activa
A6.8.1 (2)	xxxxxxx	2004	Teratology Study of the Test Item Difenacoum Technical in Rabbits xxxxxxx Report No. 03/738-105N. GLP, Unpublished	Y	PelGar and Activa
A6.8.2	xxxxxxx	2004	Two Generation Reproduction Toxicity Study of Test Item Difenacoum Technical in Rats xxxxxxx Report 03/738-202P. GLP, Unpublished	Y	PelGar and Activa
A6.12.1	xxxxxxx	2005	Letter: Health Monitoring of Workers in the Rodenticide Production Facility. Unpublished	Y	Activa
A6.12.2 (1)	Smolinske SC, Scherger DS, Kearns PS, Rumack BH	1987	Long-acting Anticoagulant Rodenticide Ingestion In Children Veterinary and Human Toxicology, 29 (6), 492. Published	N	Public Domain
A6.12.2 (2)	Barlow AM, Gay AL, Park BK	1982	Difenacoum (Neosorexa) Poisoning British Medical Journal, 285, 541. Published	N	Public Domain
A6.12.3	xxxxxxx	2001	Information about and toxicity of anticoagulant rat poisons: Case Histories from the Milan Poisons Centre 1996-1999 xxxxxxx Unpublished	Y	Activa
A6.12.5	Park BK, Choonara JA, Haynes BP, Breckenridge AM, Malia RG and Preston FE	1986	Abnormal Vitamin K Metabolism in the Presence of Normal Clotting Factor Activity in Factory Workers Exposed to 4-Hydroxymcoumarins British Journal of Clinical Pharmacology, 21, 289-294. Published	N	Public Domain
A6.12.7 A6.12.8	WHO	1995	Environmental Health Criteria 175 - Anticoagulant Rodenticides IPCS, WHO, Geneva. Published	N	Public Domain
A6.13 (1)	Bullard RW, Thompson RD and Holguin G	1976	Diphenadione Residues in Tissues of Cattle Journal of Agricultural Food Chemistry, 24 (2), 261-263. Published	N	Public Domain

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP /(Un)Unpublished	Data Protection Claimed (Yes/No)	Owner
A6.13 (2)	Veenstra GE, Owen DE and Huckle KR	1991	Metabolic and Toxicological Studies on the Anticoagulant Rodenticide, Flocoumafen. Recent Developments in Toxicology: Trends, Methods and Problems Arch. Toxicol., Suppl., 14, 160-165. Published	N	Public Domain
B6.6 (1) II-C	xxxxxxx	2004	Study to Determine Potential Exposure to Operators During Simulated Use of Anticoagulant Rodenticide Baits xxxxxxxReport No. SYN/1302. Unpublished.	Y	PelGar and Activa
B6.6 (2) II-C	xxxxxxx	2006	Estimation of the frequency of dermal exposure during the occupational use of rodenticides. Report of EBRC Consulting under contact to CEFIC Rodenticide Working Group. Unpublished.	Y	PelGar and Activa
A7.1.1.1.1	Fabbrini R	1997	Difenacoum –Determination of Abiotic Degradation Hydrolysis as a Function of pH ChemService S.p.A., Report No. CH-15/96-B-DIF. GLP, Unpublished	Y	PelGar and Activa
A7.1.1.1.2(1)	Drake RM	2004	Determination of the Direct Photolysis Rate in Water by Sunlight of Difenacoum Chemex Environmental International Ltd., Report No. ENV6767/120139. GLP, Unpublished	Y	PelGar and Activa
A7.1.1.1.2(2)	Drake R	2005	LETTER: Breakdown products with retention times for Difenacoum from the photolysis Chemex Environmental Ltd., ENV6767/120139. Unpublished	Y	PelGar and Activa
A7.1.1.1.2(3)	Gomez A	2005	Determination of the direct photolysis rate in water by sunlight of difenacoum, Proposal of Degradants Safepharm Laboratories Ltd. Unpublished	Y	PelGar and Activa
A7.1.1.2.1	Drake RM	2003	Determination of the Ready Biodegradability of Difenacoum Technical Chemex Environmental International Ltd. Report No. ENV5798/120139. GLP, Unpublished	Y	PelGar and Activa
A7.1.1.2.2	Drake RM	2005	Evaluation of the Determination of the Inherent Biodegradability of Difenacoum Chemex Environmental International Ltd., Report No., ENV7148/120139. GLP, Unpublished	Y	PelGar and Activa

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A7.1.2.1.2	Drake RM	2005	Determination of the Anaerobic Biodegradability of Difenacoum Chemex Environmental International Ltd., Report No. ENV7147/120139. GLP/Unpublished	Y	PelGar and Activa
A7.1.3	Drake RM	2005	The Estimation of the Adsorption Coefficient (Koc) of Difenacoum Chemex Environmental International Ltd., Report No. ENV7005/120139. GLP/Unpublished	Y	PelGar and Activa
A7.3.1	SafePharm Laboratories	2004	QSAR Method for Estimation of Phototransformation in Air, EPIWIN v 3.12 SafePharm Laboratories Ltd. Unpublished	Y	PelGar and Activa
A7.4.1.1	xxxxxxx	2003	The Toxicity to Rainbow Trout (*Oncorhynchus mykiss*) of Difenacoum Technical xxxxxxx Report No. ENV5794/120139. GLP, Unpublished	Y	PelGar and Activa
A7.4.1.2	Craig WJ	2001	The Toxicity to *Daphnia magna* of Difenacoum Technical Chemex Environmental International Ltd., Report No. ENV5793/120139. GLP, Unpublished	Y	PelGar and Activa
A7.4.1.3	Craig WJ	2003	The Growth Inhibition of the alga *Selenastrum capricornutum* by Difenacoum Technical Chemex Environmental International Ltd., Report -ENV5792/120139. GLP/Unpublished	Y	PelGar and Activa
A7.4.1.4	Staniland J	2005	An Evaluation of the Effect Of Difenacoum on the Inhibition of Activated Sludge Respiration According to OECD 209 Chemex Environmental International Ltd., Report No. ENV7006/120139. GLP, Unpublished	Y	PelGar and Activa
A7.4.2	SafePharm Laboratories	2004	QSAR Method for Estimation of Bioconcentration Factor, EPIWIN v 3.12 SafePharm Laboratories Ltd. Unpublished	Y	PelGar and Activa
A7.4.3.3.1	xxxxxxx	2004	The Bioconcentration Potential of Difenacoum in Rainbow Trout (*Oncorhynchus mykiss*) Under Flow-Through Conditions xxxxxxx Report No. ENV6596/120139. GLP, Unpublished	Y	PelGar and Activa

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A7.5.1.2	Staniland J	2005	The Toxicity to *Eisenia foetida foetida* of Difenacoum Chemex Environmental International Ltd., Report No. ENV7007/120139. GLP, Unpublished	Y	PelGar and Activa
A7.5.3.1.1	xxxxxxx	2005	Acute oral toxicity of Difenacoum Technical on Japanese Quail (*Coturnix coturnix japonica*) xxxxxxx Report No. 04/904-115FU. GLP, Unpublished	Y	PelGar and Activa
A7.5.3.1.2	xxxxxxx	2006	Difenacoum Technical – Dietary Toxicity Test with the Japanese Quail (*Coturnic coturnix japonica*) xxxxxxx Report No. 13768.4100. GLP, Unpublished	Y	PelGar and Activa
A7.5.3.1.3	xxxxxxx	2005	Avian Reproduction Toxicity Test of Difenacoum Technical in the Japanese Quails (*Coturnix coturnix japonica*) xxxxxxx Report No. 03/779-206FU. GLP, Unpublished	Y	PelGar and Activa
A7.5.5	SafePharm Laboratories	2004	QSAR Method for Estimation of Bioconcentration Factor, EPIWIN v 3.12 SafePharm Laboratories Ltd. Unpublished	Y	PelGar and Activa
B3.6	Capel-Williams G	2004	Study to Determine the Density of the Product Roban Wax Block PelGar International Ltd., Report No. PHYCEM/DCM/04081101. Unpublished	Y	PelGar
B3.7	Thomas KT	1999	Storage Stability and Physical-Chemical Characteristics of a 0.005% w/w Wax Block Formulation of Difenacoum School of Pure and Applied Biology, University of Wales Cardiff, Report No. 96021263. GLP, Unpublished	Y	PelGar
B4.1	Drake RM	2004	Method Validation for the Determination of Difenacoum in Whole Wheat and in Wax Block Baits Chemex Environmental International Ltd., Report No. ENV6412. GLP, Unpublished	Y	PelGar
B5	xxxxxxx	1996	Humaneness Assessment of PelGar Anticoagulant Rodenticides, Using albino Norway Rat and Albino House Mice Report No. CVS/96/047. Unpublished.	Y	PelGar
B5.10.1	PelGar		Product Label: Roban Oktablok Wax Block Bait. Unpublished.	N	PelGar

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B5.10.2 (1)	xxxxxxx	2001	Palatability and Efficacy of Aged Roban Wax Block Bait Formulation in Laboratory Mice xxxxxxx Report No. 51A/2001. GLP, Unpublished	Y	PelGar
B5.10.2 (2)	xxxxxxx	2004	Palatability and Efficacy of Aged Roban Wax Block Bait Formulation in Laboratory Rats xxxxxxx Report No. 03/2004. GLP, Unpublished	Y	PelGar
B5.10.2 (3)	xxxxxxx	2003	Palatability and Efficacy of Roban Wax Block Bait Formulation in Laboratory Rats xxxxxxx Report No. 59/2003. GLP, Unpublished	Y	PelGar
B5.10.2 (8)	Hadler MR	1975	New Rodenticides for the Control of Resistant Rats and Mice Procedures of the Fourth British Pest Control Conference, 20, pp. 1-6. Published	N	Public Domain
B5.10.2 (10)	Hadler MR, Redfern R and Rowe FP	1975	Laboratory Evaluation of Difenacoum as a Rodenticide Journal of Hygiene, 74, 441-448. Published	N	Public Domain
B5.10.2 (11)	Lund M	1981	Comparative Effect of the Three Rodenticides Warfarin, Difenacoum and Brodifacoum on Eight Rodent Species in Short Feeding Periods Journal of Hygiene, 1, 101-107. Published	N	Public Domain
B5.10.2 (14)	Wade JO	2005	Determination of Mould Growth on Standard Wax Blocks Stored Under Simulated Sewage Inspection Chamber Conditions PelGar International Ltd., Report No. PEL/01/05. Unpublished	Y	PelGar
B6.1.1	xxxxxxx	1995	Difenacoum – Acute Oral Toxicity to the Rat of a 2.5% Concentrate Xxxxxxx Report No. MLS/9985. GLP, Unpublished	Y	PelGar
B6.1.2	xxxxxxx	1995	Difenacoum – Acute Dermal Toxicity to the Rat of a 2.5% w/v Concentrate Xxxxxxx Report MLS/9760. GLP, Unpublished	Y	PelGar
B6.2	xxxxxxx	1995	Difenacoum – Eye Irritation to the Rabbit Xxxxxxx Report No. MLS/9987. GLP/Unpublished	Y	PelGar

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP /(Un)Unpublished	Data Protection Claimed (Yes/No)	Owner
B6.2 (1)	xxxxxxx	1995	Difenacoum – Skin Irritation to the Rabbit xxxxxxx Report No. MLS/9758. GLP/Unpublished	Y	PelGar
B6.4	xxxxxx	2007	In vitro absorption of difenacoum from wax block and pasta bait through human epidermis xxxxxx., Rreport No. JV2011-REG GLP/Unpublished	Y	PelGar and Activa
B6.6 (1)	xxxxxxx	2004	Study to Determine Potential Exposure to Operators During Simulated Use of Anticoagulant Rodenticide Baits xxxxxxx Report No. SYN/1302. Unpublished.	Y	PelGar and Activa
II-A 4.1.1.3.1	Mullee D	2005	Assessment of the behaviour of difenacoum in soil Safepharm laboratories Ltd.	Y	PelGar and Activa
II-B 3.3.1	TGD	2003	Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances, Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. Part II. Published	N	Public Domain
II-B 3.3.1	Larsen J	2003	Emission scenario document for biocides used as rodenticides. EUBEES. Published	N	Public Domain
B7.8.7.1	Gray A, Eadsforth CV and Dutton AJ	1994	The Toxicity of Three Second-Generation Rodenticides to Barn Owls, Pesticide Science, 42, 179-184. Published	N	Public Domain
II-C 2.4.3.5	Gray, A, Eadsforth, CV, Dutton, AJ and Vaughan, JA	1992	Toxicity of second generation rodenticides to Barn Owls. Proceedings Brighton Crop Protection Conference, 781-786. Published	N	Public Domain
II-C 2.4.3.5	Newton, I, Wyllie, I and Freestone, P	1990	Rodenticides in British Barn Owls. Environmental Pollution, 68, 101–117. Published	N	Public Domain
II-C 2.4.3.5	Mendenhall, VM and Pank, LF	1980	Secondary Poisoning of owls by anticoagulant rodenticides. The Wildlife Society Bulletin, 8, 4, 311-315. Published	N	Public Domain

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II-C 2.4.3.5	Atterby H, Kerins GM, and MacNicoll AD	20045	Whole-Carcass Residues of the Rodenticide Difenacoum in Anticougulant-Resistant and -Susceptible Rat Strains (*Rattus norvegicus*) Environmental Toxicology and Chemistry, 24 (2), 318-323. Published	N	Public Domain
II-C 2.4.3.6	Newton, I, Wyllie, I and Dale, L	1997	Mortality causes in British Barn Owls (*Tyto alba*), based on 1,101 carcasses examined during 1963-1996. In Duncan JR, Johnson DH, Nicholls TH editors. Biology and conservation of owls in the northern hemisphere, Winnipeg, Canada. United States Department of Agriculture, p. 299-307. Published	N	Public Domain
II-C 2.4.3.6	Shore, RF, Birks JDS, Afsar, A, Wienburg, CL and Kitchener, AC	2003	Spatial and temporal analysis of second-generation anticoagulant rodenticides in polecats (*Mustela putorius*) from their range in Britain, 1992-1999. Environmental Pollution 122: 183-193	N	Public Domain
II-C 2.4.3.6	Birks, JDS	1998	Secondary rodenticide poisoning risk arising from winter farmyard use by the European Polecat *Mustela putorius*. Biological Conservation 85: 233-240. Published	N	Public Domain
II-C 2.4.3.6	Fletcher, MR, Hunter, K, Barnett, EA and Sharp, EA	1999	Pesticide Poisoning of Animals 1998: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides. Published	N	Public Domain
II-C 2.4.3.6	Fletcher, MR, Hunter, K, Barnett, EA and Sharp, EA	2000	Pesticide Poisoning of Animals 1999: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides. Published	N	Public Domain
II-C 2.4.3.6	Barnett, EA, Fletche, MR, Hunter, K and Sharp, EA	2002a	Pesticide Poisoning of Animals 2000: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides. Published	N	Public Domain
II-C 2.4.3.6	Barnett, EA, Fletcher, MR, Hunter, K and Sharp, EA	2002b	Pesticide Poisoning of Animals 2001: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides. Published	N	Public Domain
II-C 2.4.3.6	Barnett, EA, Fletcher, MR, Hunter, K and Sharp, EA	2003	Pesticide Poisoning of Animals 2002: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides. Published	N	Public Domain

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II-C 2.4.3.6	Barnett, EA, Fletcher, MR, Hunter, K and Sharp, EA	2004	Pesticide Poisoning of Animals 2003: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides. Published	N	Public Domain
II-C 2.4.3.6	Barnett EA, Fletcher MR, Hunter K and Sharp EA	2005	Pesticide Poisoning of Animals 2004: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides. Published	N	Public Domain
II-C 2.4.3.6	Barnett EA, Fletcher MR, Hunter K and Sharp EA	2006	Pesticide Poisoning of Animals 2005: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides. Published	N	Public Domain
II-C 2.4.3.6	Barnett EA, Fletcher MR, Hunter K, Taylor MJ and Sharp EA	2007	Pesticide Poisoning of Animals 2006: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides. Published	N	Public Domain
II-C 2.4.3.7	Brakes, CR and Smith, RH	2005	Exposure of non-target small mammals to rodenticides: short-tem effects, recovery and implications for secondary poisoning. Journal of Applied Ecology 42: 118-128. Published	N	Public Domain

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Section No / Reference No	Author(s)	Year	Title. Source, Report No. GLP / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A2.6/01	Anonymous	2004	Outline process for the manufacture of Difenacoum [redacted], Not GLP, Not Published CONFIDENTIAL	Y (New/First)	[redacted]
A2.7/01	Anonymous	2000	Difenacoum technical: Specification No: 239 [redacted], Not GLP, Not Published CONFIDENTIAL	Y (New/First)	[redacted]
A2.7/02	Anonymous	2001	Analisys Certificate: Difenacoum Technical, batch C3S [redacted], Not GLP, Not Published CONFIDENTIAL	Y (New/First)	[redacted]
A2.7/03	M[redacted], E.	2003	Difenacoum - Preliminary HPLC Screening for Significant (>0.1% w/w) Impurities of Difenacoum Inveresk Research, Tranent, Scotland, Report No.: 23206 Not GLP, Not Published CONFIDENTIAL	Y (New/First)	[redacted]
A2.10.2/01	S[redacted], T.	2004	Estimation of distribution in the environment of Difenacoum EBRC Consulting GmbH, Hannover, Germany, Not GLP, Not Published	Y (New/First)	[redacted]
A3.1.1/01	S[redacted], H.	2001	Difenacoum purified: thermal stability - melting point/ melting range - boiling point/ boiling range Siemens Axiva, Frankfurt, Germany, Report No.: 20011213.01 GLP, Not Published	Y (New/First)	[redacted]
A3.1.3/01	S[redacted], H.	2001	Difenacoum purified: relative density Siemens Axiva, Frankfurt, Germany, Report No.: 20011213.02 GLP, Not Published	Y (New/First)	[redacted]
A3.2/01	S[redacted], H.	2001	Difenacoum purified: vapour pressure Siemens Axiva, Frankfurt, Germany, Report No.: 20011213.03 GLP, Not Published	Y (New/First)	[redacted]
A3.2.1/01	S[redacted], T.	2003	Model calculation of Henry's Law Constant of Difenacoum EBRC Consulting GmbH, Hannover, Germany, Not GLP, Not Published	Y (New/First)	[redacted]

Section No / Reference No	Author(s)	Year	Title. Source, Report No. GLP / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A3.4/01	R[redacted], S.	1996	Difenacoum: Determination of physico-chemical properties C[redacted] H[redacted] (Europe), Report No.: [redacted] GLP, Not Published	Y (New/First)	[redacted]
A3.4/02	E[redacted], D.	1996	Difenacoum: Determination of spectroscopic properties C[redacted] H[redacted] (Europe), Report No.: [redacted] GLP, Not Published	Y (New/First)	[redacted]
A3.5/01	H[redacted], A.	2002	Water Solubility of Difenacoum GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20011378/01-PCSB GLP, Not Published	Y (New/First)	[redacted]
A3.6/01	S[redacted], A.	2004	Draft report: Difenacoum technical - Dissociationconstant Siemens Axiva, Frankfurt, Germany, Report No.: 20011213.04 GLP, Not Published	Y (New/First)	[redacted]
A3.9/01	H[redacted], A.	2002	Partition Coefficient of Difenacoum (HPLC Method) GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20011378/01-PCPC GLP, Not Published	Y (New/First)	[redacted]
A3.11/01	H[redacted], A.	2004	Flammability (solids) of Difenacoum GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20011378/01-PCFS GLP, Not Published	Y (New/First)	[redacted]
A3.11/02	S[redacted], H.	2004	Difenacoum technical – Auto-flammability Siemens Axiva, Frankfurt, Germany, Report No.: 20040216.01 GLP, Not Published	Y (New/First)	[redacted]
A3.15/01	B[redacted], R.V.	2004	Explosivity of Difenacoum technical EBRC Consulting GmbH, Hannover, Germany, Report No.: HEN-040112-01 Not GLP, Not Published	Y (New/First)	[redacted]
A3.16/01	B[redacted], R.V.	2004	Oxidising properties of Difenacoum technical EBRC Consulting GmbH, Hannover, Germany, Report No.: HEN-040112-02 Not GLP, Not Published	Y (New/First)	[redacted]
A3.16/02	Y[redacted], S.	2005	Oxidising properties on a sample of Difenacoum. Chilworth Technology Ltd., Southampton, UK, Report no. GLP14238R1V1/05 GLP, Not Published	Y (New/First)	[redacted]
A4.1/01	C[redacted], W.B.; C[redacted], A.	2000	Difenacoum - Product chemistry of Difenacoum: Analytical profile of 5 batches Inveresk Research, Tranent, Scotland, Report No.: S[redacted] GLP, Not Published CONFIDENTIAL	Y (New/First)	[redacted]

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A4.2(a)/01	W[redacted], A.	2004	Residue analysis of Difenacoum in soil - method validation GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20031413/01-RVS GLP, Not Published	Y (New/First)	[redacted]
A4.2(d)/03	D[redacted], A.M; M[redacted], G.M.	2002	Development and validation of a method for determination of difenacoum in rat liver samples Inveresk Research, Tranent, Scotland, Report No.: S[redacted] GLP, Not Published	Y (New/First)	[redacted]
A4.2/05	Mundy, D.E.; Machin, A.F.	1977	Determination of the rodenticide Difenacoum in biological materials by high-pressure liquid chromatography with confirmation of identity by mass spectrometry J. Chromatography 139, 321-329, Not GLP, Published	N	
A4.2/06	Jones, A.	1996	HPLC determination of anticoagulant rodenticide residues in animal livers. Bull. Environ. Contam. Toxicol. 56, 8-15; Not GLP, Published	N	
A4.2/07	Hunter, K.	1985	High-performance liquid chromatographic strategies for the determination and confirmation of anticoagulant rodenticide residue in animal tissues J. Chromatography 321, 255-272, Not GLP, Published	N	
A4.2/08	Langseth, W.; Nymoen U.	1991	Determination of coumarin anticoagulant rodenticide residues in animal liver by high-performance liquid chromatography Fresenius J. Anal. Chem. 339, 249-252, Not GLP, Published	N	
A4.2(d)/09	Chalermchaikit, T; Felice, L.J.; Murphy, M.J.	1993	Simultaneous determination of eight anticoagulant rodenticides in blood serum and liver J. Anal. Toxicol. 17, 56-61, Not GLP, Published	N	
A4.2/10	Berny, P.J.; Buronfosse, T.; Lorgue, G.	1995	Anticoagulant poisoning in animals: a simple new high-performance thin-layer chromatographic (HPTLC) method for simultaneous determination of eight anticoagulant rodenticides in liver samples J. Anal. Toxicol. 19, 576-580, Not GLP, Published	N	
A4.2/11	Chalermchaikit, T; Felice, L.J.; Murphy, M.J.	1991	Multicomponent determination of 4-hydroxycoumarin anticoagulant rodenticides in blood serum by liquid chromatography with fluorescence detection J. Anal. Toxicol. 15, 126-129, Not GLP, Published	N	

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A4.2(c)/12	S[redacted], G.C et al.	2005	Development and Validation of a Method for the Determination of Difenacoum in Surface Water. Charles River Laboratories, Report Number: 26056 GLP, Not Published	Y (New/First)	[redacted]
A4.2 (c)/13	S[redacted], G.C., D[redacted], J.	2005	Development and Validation of a Method for the Determination of Difenacoum in Sediment. Charles River Laboratories, Report Number: 25986 GLP, Not Published	Y (New/First)	[redacted]
A4.3/03	K[redacted], S.	2006	Validation of multi-residue method DFG S19 (L 00.00-34) for the determination of residues of Difenacoum in different plant matrices and meat with LC-MS/MS detection. Eurofins Analytik GmbH, Dr. Specht Laboratorien, Hamburg, Germany, Report no. H[redacted] GLP, Not Published	Y (New/First)	[redacted]
A5.3/01	Bradfield, A.A.G.; Gill, J.E.	1984	Laboratory trials of five rodenticides for the control of Mesocricetus auratus Waterhouse J. Hyg. 93, 389-394, Not GLP, Published	N	
A5.3/02	Gill, J.E.; Redfern, R.	1980	Laboratory trials of seven rodenticides for use against the cotton rat (Sigmodon hispidus) J. Hyg. 85, 443-450, Not GLP, Published	N	
A5.3/03	Bäumler, W.; Asran, A.A.	1987	Empfindlichkeit von Hausmäusen verschiedener Herkunft gegen Antikogulantien Anz. Schädlingskd. Pflanzensch. Umweltsch. 60, 1-6, Not GLP, Published	N	
A5.3/04	Gill, J.E.; Redfern, R.	1977	Some laboratory Tests of five rodenticides for the contral of Arvicanthis niloticus PANS 23, 33-37, Not GLP, Published	N	
A5.3/05	Mahmoud, W.; Redfern, R.	1981	The response of the Egyptian spiny mouse (Acomys cahirinus) and two other species of commensal rodents to antigoagulant rodenticides J. Hyg. 86, 329-334, Not GLP, Published	N	
A5.3/06	Gill, J.E.; Redfern, R.	1983	Laboratory tests of seven rodenticides for the control of Meriones Shawi J. Hyg. 91, 351-357, Not GLP, Published	N	

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A5.3/07	Rowe, F.P.; et al.	1980	Comparative acute and chronic toxicity tests on confined colonies of wild house mice Biol. BA Land-/Forstw. 50/16, Not GLP, Published	N	
A5.3/08	Hadler, M.R.; et al.	1975	Laboratory evaluation of difenacoum as a rodenticide J. Hyg. 74, 441-448, Not GLP, Published	N	
A5.3/09	Rennison, B.D.; Hadler, M.R.	1975	Field trials of difenacoum against warfarin-resistant infestations of Rattus norvegicus J. Hyg. 74, 449-455, Not GLP, Published	N	
A5.3/10	Rowe, F.P.; et al.	1981	Trials of the anticoagulant rodenticides bromadiolone and difenacoum against the house mouse(mus musculus l.) J. Hyg. 87, 171-177, Not GLP, Published	N	
A5.3/11	Rowe, F.P.; Swinney, T.	1988	The efficacy of two permanent poison-baiting measures against mus domesticus living in farm buildings in the UK EPPO Bull. 18, 229-235, Not GLP, Published	N	
A5.3/12	Bull, J.O.	1976	Laboratory and field investigations with difenacoum, apromising new rodenticide Proceedings of the 77th Vertebrate Pest Conference, Monterey, California, University of California, 72-84, Not GLP, Published	N	
A5.3/13	Hadler, M.R.	1975	A weapon against the resistant rat Pesticides 9, 63-65, Not GLP, Published	N	
A5.3/14	Hadler, M.R.	1976	Un arma contra la rata resistente Ciencias 41, 197-200, Not GLP, Published	N	
A5.4/01	Thijssen, H.H.W.	1995	Warfarin-based rodenticides: Mode of action and mechanism of resistance Pestic. Sci. 43, 73-78, Not GLP, Published	N	
II-A 2.3.3	Pesticides Safety Directorate	1997	Assessment of humaneness of vertebrate control agents. (Food and environment protection act, 1985, part III, control of pesticides regulations 1986, Evaluation of fully approved or provisionally approved products, Issue 171; York YO1 7PX)	N	
II-A 2.3.3	Anon	1992	Anticoagulant Rodenticide Humaneness Data Overview Part 1 and Part 2. Not GLP, unpublished. GR-959-0075	Yes	[redacted]
A5.7.1/01	Pelz, H.-J.; et al.	1995	Resistance to anticoagulant rodenticides in Germany and future strategies Pestic. Sci. 43, 61-67, Not GLP, Published	N	

Section No / Reference No	Author(s)	Year	Title. Source, Report No. GLP / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A5.7.1/02	Pelz, H.-J.; et al.	1992	Resistenz gegenüber Wirkstoffen aus der Gruppe der Antikoagulantien bei Wanderratten in Nordwestdeutschland Mitt. Biol. Bundesanstalt Land. Forst. 283, 200, Not GLP, Published	N	
A5.7.1/03	Quy, R.J.; et al.	1992	Bait avoidance and effectiveness of anticoagulant rodenticides against warfarin- and difenacoum-resitant populations of Norway rats (ratus norvegicus) Crop Protection 11, 14-20, Not GLP, Published	N	
A5.7.1/04	Greaves, J.H.; et al.	1982	Field trials of second-generation anticuagulants against difenacoum-resistant norway rat populations J. Hyg. 89. 295-301, Not GLP, Published	N	
A5.7.1/05	Greaves, J.H.; et al.	1982	An investigation of difenacoum resistence in Norway rat populations in Hampshire Ann. Appl. Biol. 100, 581-587, Not GLP, Published	N	
A5.7.1/06	Quy, R.J.	1995	Controlling a population of norway rats resistant to anticoagulant rodenticides Pestic. Sci. 45, 247-256, Not GLP, Published	N	
A5.7.1/07	Meehan, A.P.	1984	Rats and mice - their biology and control Rentokil Ltd., East Grinstead, UK, Not GLP, Published	N	
A5.7.1/08	Hadler, M.R.	1992	Second generation anticoagulant rodenticides: their effectivesness and economics Pest. Outlook 3, 25-28, Not GLP, Published	N	
A5.7.1/09	Hildebrandt, E.F., Suttie, J.W.	1982	Mechanism of coumarin action: sensitivity of vitamin K metabolizing enzymes of normal and Warfarin-resistant rat liver Biochem. 21, 2406-2411, Not GLP, Published	N	
A5.7.1/10	Cowan, D.; et al.	1995	The impact of resistance on the use of second-generation anticoagulants against rats on farms in Southern England Pestic. Sci. 43, 83-93, Not GLP, Published	N	
A5.7.1/11	Quy, R.J.; et al.	1992	The influence of stored food on the effectiveness of farm rat control Proceedings Brighton Crop Protection Conference – Pests and Diseases – 1992, 291-300, Not GLP, Published	N	

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A5.7.1/12	MacNicoll, A.D.	1988	The role of altered vitamin K metabolism in anticoagulant in rodents Suttie, J.W. (ed.): Current Advances in Vitamin K research - A Steenbock Symposium, Elsevier, 407-417, Not GLP, Published	N	
A5.7.1/13	Greaves, J.H.; Cullen-Ayres, P.B.	1988	Genetics of Difenacoum resistence in the rat Suttie, J.W. (ed.): Current Advances in Vitamin K research - A Steenbock Symposium, Elsevier, 389-397, Not GLP, Published	N	
A5.7.1/14	Lund, M.	1988	Detection and monitoring of resistance to anticoagulant rodenticides in populations of brown rats (Rattus norvegicus) in Denmark Suttie, J.W. (ed.): Current Advances in Vitamin K research - A Steenbock Symposium, Elsevier, 399-405, Not GLP, Published	N	
A5.7.1/15	Desideri D.; et al.	1979	La résistance murine aux anticoagulants dans le port de Marseille (suite) - état de réponse au Difénacoum Bull. Soc. Pathol. Exotique 72, 278-283, Not GLP, Published	N	
A5.7.1/16	Bäumler, W.	1985	Über die Wirksamkeit verschiedener Antikoagulantinen gegen schädliche Nagetiere Anz. Schädlingskde., Pflanzenschutz, Umweltschutz 58, 90-93, Not GLP, Published	N	
A5.7.1/17	Anonymous	1999	Physiological resistance to rodenticides Int. Pest Control 41, 187-190, Not GLP, Published	N	
A5.7.1/18	Jackson, W.B.; et al.	1988	Overview of anticoagulant rodenticide usage and resistance Suttie, J.W. (ed.): Current Advances in Vitamin K research - A Steenbock Symposium, Elsevier, 381-388, Not GLP, Published	N	
A5.7.1/19	Smith R.H.;Greaves J.H.	1986	Resistance to anticoagulant rodenticides: the problem and its management Phytoparasitica 14, 355, Not GLP, Published	N	
A5.7.2/01	Anonymous	2003	Anticoagulant resistance management strategy for pest management professionals, central and local government and other competent users of rodenticides Tech. Monograph, CropLife Intl., Brussels, Belgum, Not GLP, Published	N	

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A5.7.2/02	Greaves, J.H.	1995	Managing resistance to anticoagulant rodenticides: an appraisal Pestic. Sci. 43, 79-82, Not GLP, Published	N	
A5.7.2/03	Pelz, H.-J.	1991	Resistenzen gefährden den Bekämpfungserfolg Prakt. Schädlingsbek. 43, 177-179, Not GLP, Published	N	
A5.7.2/04	Prescott, C.V.	2003	A reappraisal of blood clotting response tests for anticoagulant resistance and a proposal for a standardised BCR test methology Tech. Monograph, CropLife Intl., Brussels, Belgum, Not GLP, Published	N	
A5.7.2/05	MacNicoll, A.D.; Gill, J.E.	1993	Vitamin K3 in feedstuffs: antidotal effects in captive anticoagulant-resistant rats and mice J. Wildl. Manage. 57, 835-841, Not GLP, Published	N	
A5.7.2/06	Gill, J.E.; et al.	1993	The development of a blood clotting response test for discriminating between difenacoum-resistant and susceptible Norway rats (Rattus norvegicus, Berk.) Comp. Biochem. Physiol. 104C, 29-36, Not GLP, Published	N	
A5.7.2/07	Redfern, R.; Gill, J.E.	1978	The development and use of a test to identify resistance to the anticoagulant Difenacoum in the Norway rat (Rattus norvegicus) J. Hyg. 81, 427-431, Not GLP, Published	N	
A5.7.3/01	Smith, P.; et al.	1994	Symptom-dependent taste aversion induced by an anticoagulant rodenticide in the brown rat (Rattus norvegicus) J. Comp. Psychol. 108, 282-290, Not GLP, Published	N	
Doc II-A, 2.4	Li T, Chang C-Y, Jin D-Y, Lin P-J, Khvorova A and Stafford DW	2004	Identification of the gene for vitamin K epoxide reductase. Nature 427: 541-544.	N	

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Doc II-A, 2.4	Rost S, Fregin A, Ivankevicius V, Conzelmann E, Hörtnagel K, Pelz H-J, Lappegard K, Seifred E, Scharrer I, Tuddenham EGD and others	2004	Mutations in VKORC1 cause warfarin resistance in multiple coagulation factor deficiency type 2. Nature 427: 537-541.	N	
Doc II-A, 2.4	Pelz H-J, Rost S, Hünerberg M, Fregin A, Heiberg A-C, Baert K, MacNicoll AD, Prescott CV, Walker A-S, Oldenburg J and Müller CR	2005	The genetic basis of resistance to anticoagulants in rodents. Genetics, published on May 6, 2005 as 10.1534/genetics.104.040360.	N	
A6.1.1/01	[redacted]	2002	Acute toxicity study of Difenacoum technical by oral administration to sprague-dawley rats [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.1.1/02	R[redacted], M. C.	1998	Acute Oral Toxicity (LD_{50}) Tests with Cis- and Trans-isomers and a Racemic Mixture of Difenacoum B[redacted] Report No.: 3175/2/2/98 [redacted]. GLP, Not Published	Y (New/First)	[redacted]
A6.1.1/03	G[redacted], J. R.	1995a	Difenacoum: Acute Oral Toxicity Study in the Male Wistar Rat C[redacted] H[redacted] (Europe), Report no: 355/34-1032. GLP, Not Published. [D[redacted]-959-0011].	Y (New/First	[redacted]
A6.1.2/01	[redacted]	2002	Acute toxicity study of Difenacoum technical in sprague-dawley rats by dermal administration [redacted] GLP, Not Published	Y (New/First)	[redacted]

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A6.1.2/02	G[redacted], J. R.	1995d	Difenacoum: Acute Dermal Toxicity Study in the Rat. H[redacted] Europe, Report No: 355/9-1032. GLP, unpublished. [redacted].	Y (New/First	[redacted]
A6.1.3/01	[redacted]	1996	Difenacoum: Single dose inhalation (head-only) toxicity study in the rat [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.1.4/01	[redacted]	2002	Acute skin irritation test (patch test) of Difenacoum technical in rabbits [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.1.4/02	[redacted]	2002	Acute eye irritation study of Difenacoum technical by instillation into the conjunctival sac of rabbits [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.1.5/01	[redacted]	2002	Examination of Difenacoum technical in a skin sensitisation test in guinea-pigs according to Magnusson and Kligman (maximisation test) [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.2/01	[redacted]	2002	An investigation into the elimination and tissue distribution of the 14C-labelled stereoisomers of difenacoum following oral administration to rats [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.2/02	[redacted]	1996	An investigation into the absorption, tissue distribution and elimination of 14C-labelled difenacoum following oral administration to rats [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.2/03	[redacted]	1987	Difenacoum: Elimination from the tissues of rats following administration of a single oral dose [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.3.1/01	[redacted]	2003	4-week dose range-finding study for a 90-day subchronic toxicity study of Difenacoum technical by repeated oral administration to sprague-dawley rats [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.4.1/01	[redacted]	2003	90-day subchronic toxicity study of Difenacoum technical by repeated oral administration to CD rats [redacted] GLP, Not Published	Y (New/First)	[redacted]

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A6.5/01 A6.12.5/02 A6.12.7/02 A6.12.8/01	WHO/ICPS	1995	Environmental health criteria 175: anticoagulant rodenticides WHO, Genf, Switzerland, Not GLP, Published	N	
A6.6.1/01	[redacted]	2002	Mutagenicity study of Difenacoum technical in the Salmonella typhimurium reverse mutation assay (in vitro [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.6.2/01	[redacted]	2002	In vitro assessment of the clastogenic activity of Difenacoum technical in cultured human peripheral lymphocytes [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.6.3/01	[redacted]	2002	Mutagenicity study of Difenacoum technical in mammalian cells (V79) in the in vitro gene mutation assay (HPRT test) [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.6.4/01	R[redacted], S.	1996	Difenacoum: Induction of Micronuclei in the Bone Marrow of Treated Rats. C[redacted] Report No: 355/37-1052. GLP, Not Published. [[redacted]].	Y (New/First)	[redacted]
A6.6.4/02	S[redacted], T., R[redacted], C. R., R[redacted], V. and H[redacted], D.	1987	Difenacoum: An Evaluation in the Mouse Micronucleus Test. I[redacted], Report No: CTL/P/1666. GLP, Not Published. [C2.6/03].	Y (New/First)	[redacted]
A6.6.5/01	C[redacted], C.	1996	Difenacoum: Measurement of Unscheduled DNA Synthesis in Rat Liver Using an In Vivo/In Vitro Procedure. C[redacted] Report No: 355/38-1052. GLP, Not Published. [[redacted]].	Y (New/First)	[redacted]
A6.8.1/01	[redacted]	1994	Difenacoum: Development toxicity study in the rat [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.8.1/02	[redacted]	1994	Difenacoum: Development toxicity study in the rabbit [redacted] GLP, Not Published	Y (New/First)	[redacted]
A6.12.1/01	[redacted]	2004	Arbeitsmedizinische Untersuchungen am 27.11.2003 [redacted] Not GLP, Not Published	Y (New/First)	[redacted]

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A6.12.1/02	B[redacted], C.	2004	Arbeitsmedizinische Untersuchungen 17.8. 2004. [redacted] Not GLP, Not Published	Y (New/First)	[redacted]
A6.12.2/01 A6.12.4/01	Ingels, M.; et al.	2002	A prospective study of acute, unintentional, pediatric superwarfarin ingestions managed without decontamination Annals Emerg. Med. 40, 73-78, Not GLP, Published	N	
A6.12.2/02	Butcher, G.P.; et al.	1992	Difenacoum poisoning as a cause of haematuria Hum. Exp. Toxicol. 11, 553-554, Not GLP, Published	N	
A6.12.2/03	Nighoghossian, N.; et al.	1990	Hématome sous-dural cervico-dorsal par intoxication aux raticides coumariniques Rev. Neurol. 146, 221-223, Not GLP, Published	N	
A6.12.2/04	Barlow, A.M.; et al.	1982	Difenacoum (Neosorexa) poisoning Brit. Med. J. 285, 541, Not GLP, Published	N	
A6.12.2/05	McCarthy, P.T.; et al.	1997	Covert poisoning with difenacoum: clinical and toxicological observations Hum. Exp. Toxicol. 16, 166-170, Not GLP, Published	N	
A6.12.2/06	Smolinske, S.C.; et al.	1989	Superwarfarin poisoning in children: a prospective study Pediatrics 84, 490-494, Not GLP, Published	N	
A6.12.5/01	Mullins, M.E.; et al.	2000	Unintentional pediatric superwarfarin exposure: do we really need a prothrombin time? Pediatrics 105, 402-404, Not GLP, Published	N	
A6.12.7/01	Kanabar, D.; Volans, G.	2002	Accidental superwarfarin poisoning in children - less treatment is better Lancet 360, 963, Not GLP, Published	N	
A6.13/01	P[redacted], G.R.	1975	Difenacoum: Acute oral toxicity I[redacted]., Report No.: [redacted]: C2.1/10 GLP, Not Published	Y (New/First)	[redacted]
A6.13/02	R[redacted], D.B.; R[redacted], N.L.	1974	The acute oral toxicity of WB 8107 to the domestic pig S[redacted], Report No.: [redacted]: C2.1/07 GLP, Not Published	Y (New/First)	[redacted]
A6.13/03	H[redacted], M.R.	1975	The acute toxicity of Difenacoum to female Guinea pigs W[redacted]., Report No.: [redacted]: C2.1/11 GLP, Not Published	Y (New/First)	[redacted]

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A6.13/04	H[redacted], M.R.	1973	Acute oral toxicity of WBA 8107 to male albino rabbits W[redacted] Report No.: [redacted]: C2.1/15 GLP, Not Published	Y (New/First)	[redacted]
A7.1.1.1.1/01	H[redacted], A.	2002	Abiotic degradation of Difenacoum - hydrolysis as a function of ph GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20011378/01-PCHY GLP, Not Published	Y (New/First)	[redacted]
A7.1.1.1.2/01	H[redacted], B.E.; et al.	1992	Difenacoum: Photolysis on buffered Aqueous solutions Inveresk Research, Tranent, Scotland, Report No.: [redacted]: F4.1/02 GLP, Not Published	Y (New/First)	[redacted]
A7.1.1.2.1/01	D[redacted], D.	2002	Assessment of the ready biodegradability of Difenacoum with the closed bottle test GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20011378/01-AACB GLP, Not Published	Y (New/First)	[redacted]
A7.1.1.2.1/02	D[redacted], D.	2005	Assessment of the ready biodegradability of Difenacoum with the closed bottle test. GAB, Niefern-Öschelbronn, Germany, Report No.: 20011378/02-AACB, June 20/2005. GLP, Not Published	Y (New/First)	[redacted]
A7.1.1.2.1/03	S[redacted], M.	2005	Manometric Respirometry Test (according to EC method C.4-D and OECD 301 F) – Test item: Difenacoum. Fraunhofer-Institute for Molecular Biology and Applied Ecology, Schmallenberg, Germany, Report no. [redacted] 001 / 3-15, May 17, 2005 (unpublished).	Y (New/First)	[redacted]
A7.1.2.1.2/01	P[redacted], A.J.	2004	Difenacoum: Determination of anaerobic biodgradability A[redacted] Laboratory, Report No.: BL7788/B GLP, Not Published	Y (New/First)	[redacted]
A7.1.3/01	H[redacted], A.	2002	Adsorption-coefficient on soil of Difenacoum - sceening test by HPLC GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20011378/01-PCAD GLP, Not Published	Y (New/First)	[redacted]
A7.3.1/01	B[redacted], M.	2003	Estimation of the photochemical oxidative degradation rate in the atmosphere of Difenacoum EBRC Consulting GmbH, Hannover, Germany, Report No.: HEN-031114-01 Not GLP, Not Published	Y (New/First)	[redacted]

Section No / Reference No	Author(s)	Year	Title. Source, Report No. GLP / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A7.4.1.1/01	H[redacted], A.	2002	Acute toxicity testing of Difenacoum in rainbow trout (oncrhynchus mykiss) (teleostei, salmonidae) [redacted], Germany, Report No.: 20011378/01-AAOm GLP, Not Published	Y (New/First)	[redacted]
A7.4.1.1/02	W[redacted] LE	1995	Difenacoum: Acute Toxicity to Oncorhynchus mykiss. C[redacted] (Europe) Laboratory, Report Number: 355/17-1018. GLP, unpublished. [DF-959-0030].	Y	[redacted]
A7.4.1.2/01	H[redacted], A.	2002	Assessment of toxic effects of Difenacoum on Daphnia magna using the 48h acute immobilisation test [redacted], Germany, Report No.: 20011378/01-AADm GLP, Not Published	Y (New/First)	[redacted]
A7.4.1.3/01	D[redacted], D.	2002	Testing of toxic effects of Difenacoum on teh single cell green alga Desmodesmus subspicatus [redacted], Germany, Report No.: 20011378/01-AADs GLP, Not Published	Y (New/First)	[redacted]
A7.4.1.4/01	D[redacted], D.	2002	Acute toxicity testing of Difenacoum on activated sludge with the respiration inhibition test [redacted], Germany, Report No.: 20011378/01-AAHT GLP, Not Published	Y (New/First)	[redacted]
A7.5.3.1.1/01	N[redacted], S.	1997	Difenacoum: Acute oral toxicity to mallard duck C[redacted] Report No.: [redacted]-959-0042 GLP, Not Published	Y (New/First)	[redacted]
A7.5.3.1.1/02	R[redacted], D.B.; et al.	1980	The acute oral toxicity (LD50) of difenacoum to the bobwhite quail H[redacted], Report No.: [redacted]: G2.1/03 GLP, Not Published	Y (New/First)	[redacted]
A7.5.3.1.2/01	N[redacted], S.	2000	Difenacoum: Acute dietary toxicity to bobwhite quail C[redacted] Report No.: [redacted]-959-0043 GLP, Not Published	Y (New/First)	[redacted]
A7.5.3.1.3/01	B[redacted], J.	2005	Avian reproduction study with Difenacoum in the Japanese quail (*Coturnix coturnix japonica*). [redacted], Report no. 04012 GLP, Not Published	Y (New/First)	[redacted]

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A8/01	Anonymous	2002	Safety data sheet: Difenacoum technical material [redacted], Not GLP, Published	N	
A8.5.1/01	Anonymous	2004	Sorex difenacoum CAS No [56073-07-05] [redacted] Not GLP, Not Published	Y (New/First)	[redacted]
B2.2/01	T[redacted], M.	2003	Myocurattin-FCM-Granulat, Rezeptur Hentschke & Sawatzki KG, Neumünster, Germany, Not GLP, Not Published CONFIDENTIAL	Y (New/First)	[redacted]
B2.2/01	T[redacted], M.	2003	Myocurattin-Kanal-Diskus, Rezeptur Hentschke & Sawatzki KG, Neumünster, Germany, Not GLP, Not Published CONFIDENTIAL	Y (New/First)	[redacted]
B3.1/01	W[redacted], W.	2004	Physico-chemical properties of the solid bait "Myocurattin-Kanal-Diskus" when stored in commercial packaging material over a period of 2 years at 20 C -starting date report- GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20031414/01-PCTY GLP, Not Published	Y (New/First)	[redacted]
B3.1/01	W[redacted], W.	2004	Physico-chemical properties of the grain bait "Myocurattin-FMC-Granulat" when stored in commercial packaging material over a period of 2 years at 20 C -starting date report- GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20031415/01-PCTY GLP, Not Published	Y (New/First)	[redacted]
B3.6/01	W[redacted], W.	2004	Relative density of the solid bait “Myocurattin-Kanal-Diskus” GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20031414/01-PCTD GLP, Not Published	Y (New/First)	[redacted]
B3.6/01	W[redacted], W.	2004	Pour and tap density (CIPAC MT 159) of the grain bait “Myocurattin-FCM-Granulat” GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20031415/01-PCTD GLP, Not Published	Y (New/First)	[redacted]
B3.7/01	W[redacted], W.	2004	Physico-chemical properties of the solid bait Myocurattin-Kanal-Diskus before and after accelerated storage at 40 C for 8 weeks GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20031414/01-PCAS GLP, Not Published	Y (New/First)	[redacted]

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B3.7/01	W[redacted], W.	2004	Physico-chemical properties of grain bait "Myocurattin-FMC-Granulat" before and after accelerated storage at 54 C for 2 weeks GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20031415/01-PCAS GLP, Not Published	Y (New/First)	[redacted]
B4.1/01	W[redacted], W.	2004	Development and Validation of an analytical method for the determination of the content of active ingredient in the grain bait "Myocurattin-Kanal-Diskus" GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20031414/01-PCVE GLP, Not Published	Y (New/First)	[redacted]
B4.1/01	W[redacted], W.	2004	Development and Validation of an analytical method for the determination of the content of active ingredient in the grain bait "Myocurattin-FCM-Granulat" GAB & IFU, Niefern-Öschelbronn, Germany, Report No.: 20031415/01-PCVE GLP, Not Published	Y (New/First)	[redacted]
B5/01	Anonymous		Instruction leaflet – Myocurattin-FCM-Granulat Hentschke & Sawatzki KG, Neumünster, Germany Not GLP, Not publsihed	N	
B5/01	Anonymous		Instruction leaflet – Myocurattin-Kanal-Diskus Hentschke & Sawatzki KG, Neumünster, Germany Not GLP, Not publsihed	N	
B5.10.2/01	I[redacted], I.	2001	Gutachtliche Äußerung: Myocurattin-Kanal-Diskus UBA, Berlin, Germany, Not GLP, Not Published	Y (New/First)	[redacted]
B5.10.2/01	I[redacted], I.	1999	Gutachtliche Äußerung: Myocurattin-FCM-Granulat (Wanderratte; Raum, Tierstall, Freiland) [redacted], Not GLP, Not Published	Y (New/First)	[redacted]
B5.10.2/02	I[redacted], I.	2000	Gutachtliche Äußerung: Myocurattin-FCM-Festköder (Wanderratte; Raum, Tierstall, Freiland) [redacted], Not GLP, Not Published	Y (New/First)	[redacted]
B5.10.2/03	I[redacted], I.	2000	Gutachtliche Äußerung: Myocurattin-FCM-Festköder (Hausratte; Raum einschl. Tierstall) [redacted], Not GLP, Not Published	Y (New/First)	[redacted]

Section No / Reference No	Author(s)	Year	Title. Source, Report No. GLP / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B5.10.2/04	B[redacted], M.; I[redacted], I.	2000	Gutachtliche Äußerung: Myocurattin-FCM-Festköder (Hausmaus; Raum einschl. Tierstall) [redacted], Not GLP, Not Published	Y (New/First)	[redacted]
B6.4/01	D[redacted], D.J.	2005	50ppmDifenacoum Pellet Bait: *In vitro* absorption of difenacoum through human epidermis. C[redacted] Report No. CTL/JV1861. GLP, unpublished.	Y (New/First)	[redacted]
B6.4/02	W[redacted], R.J. and J[redacted], L.	2006	0.5% Difenacoum liquid master: *in vitro* absorption of difenacoum through human epidermis. Central Toxicology Laboratory Report No. CTL/JV1915. GLP, unpublished. [DL-6.4-0416]	Y (New/First)	[redacted]
B6.6/01	B[redacted], M.	2004	Estimation of human exposure to Difenacoum from application of "Myocurattin-FCM-Granulat" grain bait EBRC Consulting GmbH, Hannover, Germany, Report No.: HEN-040306-01 Not GLP, Not Published	Y (New/First)	[redacted]
B6.6/01	B[redacted], M.	2004	Estimation of human exposure to Difenacoum from application of "Myocurattin-Kanal-Diskus" wax blocks EBRC Consulting GmbH, Hannover, Germany, Report No.: HEN-040306-02 Not GLP, Not Published	Y (New/First)	[redacted]
B6.6/02	K[redacted], C.	2002	Rodenticides - petterns of use survey Health & Safety Laboratory, Sheffield, UK, Report No.: FSSU/02/03 Not GLP, Published	N	
B6.6/03	[redacted] J.G.	2004	Study to determine potential exposure to operators during simulated use of anticoagulant rodenticide baits Synergy Labs Ltd., Essex, UK, Report No.: SYN/1302 GLP, Not Published	Y (New/First)	[redacted]
B6.6/04	V[redacted], D. and S[redacted], T.	2006	Estimation of the frequency of dermal exposure during the occupational use of rodenticides. Report of EBRC Consulting under contact to CEFIC Rodenticide Working Group	Y (New/First)	[redacted]
B7.1/01	S[redacted], T.	2004	Estimation of environmental exposure to Difenacoum following application of "Myocurattin-FMC-Granulat" -EUBEES calculations- EBRC Consulting GmbH, Hannover, Germany, Report No.: HEN-040311-01 Not GLP, Not Published	Y (New/First)	[redacted]

Section No / Reference No	Author(s)	Year	Title. Source, Report No. GLP / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B7.1/01	S[redacted], T.	2004	Estimation of environmental exposure to Difenacoum following application of "Myocurattin-Kanal-Diskus" -EUBEES calculations- EBRC Consulting GmbH, Hannover, Germany, Report No.: HEN-040311-02 Not GLP, Not Published	Y (New/First)	[redacted]
B7.1/02	S[redacted], T.	2004	Estimation of predicted environmental concentrations of Difenacoum following application in sewage systems -EUSES report- EBRC Consulting GmbH, Hannover, Germany, Report No.: HEN-040303-01 Not GLP, Not Published	Y (New/First)	[redacted]
B7.8.7.1/01	Eadsforth, C.V.; et al.	1996	Monitoring the exposure of barn owls to second-generation rodenticides in southern eire Pestic. Sci. 47, 225-233, Not GLP, Published	N	
B7.8.7.2/01	Gray, A.; et al.	1994	Non-invasive method for monitoring the exposure of barn owls to second-generation rodenticides Pestic. Sci. 41, 339-343, Not GLP, Published	N	
B7.8.7.2/02	Gray, A.; et al.	1994	The toxicity of three second-generation rodenticides to barn owls Pestic. Sci. 42, 179-184, Not GLP, Published	N	
B7.8.7.2/03	Gray, A.; et al.	1992	Toxicity of second generation rodenticides to barn owls Proceedings Brighton Crop Protection Conference – Pests and Diseases – 1992, 781-786, Not GLP, Published	N	
B7.8.7.2/04	Mendenhall, V.M.; Pank, L.F.	1980	Secondary poisoning of owls by anticoagulant rodenticides Wildl. Soc. Bull. 8, 311-315, Not GLP, Published	N	
B7.8.7.2/05	Newton, I.; et al.	1990	Rodenticides in british barn owls Environ. Pollut. 68, 101-117, Not GLP, Published	N	
B7.8.7.2/06	Joermann, G.	1998	A review of secondary-poisoning studies with rodenticides EPPO Bull. 28, 157-176, Not GLP, Published	N	
B7.8.7.2/07	Wyllie, I.	1995	Potential secondary poisoning of barn owls by rodenticides Pest. Outlook 6, 19-25, Not GLP, Published	N	

Section No / Reference No	Author(s)	Year	Title. Source, Report No. GLP / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B7.8.7.2/08	Shore, R.F.; et al.	1996	Second-generation rodenticides and polecats (Mustela putorius) in Britain Environ. Pollut. 91, 279-282, Not GLP, Published	N	
B7.8.7.2/11	Robben, J.H.; et al.	1997	Poisoning of dogs in the Netherlands with antigoagulant rodenticides Tijdschrift Diergeneeskunde 122, 466-471, Not GLP, Published	N	
B7.8.7.2/12	Robben, J.H.; et al.	1998	Plasma superwarfarin levels and vitamin K1 treatment in dogs with anticoagulant rodenticide poisoning Vet. Quarterly 20, 24-27, Not GLP, Published	N	
B7.8.7.2/13	McDonald, R.A.; et al.	1998	Anticoagulant rodenticides in stoats (Mustela erminea) and weasels (Mustela nivalis) in England Environ. Pollut. 103, 17-23, Not GLP, Published	N	
B8/01	Anonymous	2004	Safety data sheet - Myocurattin-FCM-Granulat Hentschke & Sawatzki KG, Neumünster, Germany, Not GLP, Published	N	[redacted]
B8/01	Anonymous	2004	Safety data sheet - Myocurattin-Kanal-Diskus Hentschke & Sawatzki KG, Neumünster, Germany, Not GLP, Published	N	[redacted]
II-B 3.3.1 II-C 2	Anon	2003	Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances, Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. Part II.	N	
II-B 3.3.1 II-C 2	Larsen J	2003	Emission scenario document for biocides used as rodenticides. EUBEES.	N	
II-C 2.4.2.3	Fletcher MR, Hunter K and Barnett EA	1993	Pesticide Poisoning of Animals 1993: Investigations of Suspected Incidents in the United Kingdom. Central Science Laboratory, Ministry of Agriculture, Fisheries and Food, Slough, and Scottish Agricultural Science Agency, The Scottish Agriculture and Fisheries Department.	N	

Section No / Reference No	Author(s)	Year	Title. Source, Report No. GLP / (Un)Published	Data Protection Claimed (Yes/No)	Owner
II-C 2.4.2.3	Fletcher MR, Hunter K and Barnett EA	1995	Pesticide Poisoning of Animals 1994: Investigations of Suspected Incidents in the United Kingdom Central Science Laboratory, Ministry of Agriculture, Fisheries and Food, Slough, and Scottish Agricultural Science Agency, The Scottish Agriculture and Fisheries Department.	N	
II-C 2.4.2.3	Fletcher MR, Hunter K, Barnett EA, and Sharp EA	1996	Pesticide Poisoning of Animals 1995: Investigations of Suspected Incidents in the United Kingdom. Central Science Laboratory, Ministry of Agriculture, Fisheries and Food, Slough, and Scottish Agricultural Science Agency, The Scottish Agriculture and Fisheries Department.	N	
II-C 2.4.2.3	Fletcher MR, Hunter K, Barnett EA, and Sharp EA	1997	Pesticide Poisoning of Animals 1996: Investigations of Suspected Incidents in the United Kingdom. Central Science Laboratory, Ministry of Agriculture, Fisheries and Food, York and Scottish Agricultural Science Agency, The Scottish Office Agriculture and Fisheries Department.	N	
II-C 2.4.2.3	Fletcher MR, Hunter K, Barnett EA, and Sharp EA	1998	Pesticide Poisoning of Animals 1997: Investigations of Suspected Incidents in the United Kingdom. Central Science Laboratory, Ministry of Agriculture, Fisheries and Food, York and Scottish Agricultural Science Agency, The Scottish Office Agriculture and Fisheries Department.	N	
II-C 2.4.2.3	Fletcher MR, Hunter K, Barnett EA, and Sharp EA	1999	Pesticide Poisoning of Animals 1998: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	N	
II-C 2.4.2.3	Fletcher MR, Hunter K, Barnett EA, and Sharp EA	2000	Pesticide Poisoning of Animals 1999: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	N	
II-C 2.4.2.3	Fletcher MR, Hunter K, Barnett EA, and Sharp EA	2002a	Pesticide Poisoning of Animals 2000: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	N	
II-C 2.4.3.3	Atterby H, Kerins GM and MacNicoll AD	2005	Whole-carcass residues of the rodenticide difenacoum in anticoagulant-resistant and –susceptible rat strains (*Rattus norvegicus*). Environmental Toxicology and Chemistry 24: 318-323.	N	

Section No / Reference No	Author(s)	Year	Title. Source, Report No. GLP / (Un)Published	Data Protection Claimed (Yes/No)	Owner
II-C 2.4.3.4	Newton I, Wyllie I and Dale L	1997	Mortality causes in British Barn Owls (*Tyto alba*), based on 1,101 carcasses examined during 1963-1996. In Duncan JR, Johnson DH, Nicholls TH editors. Biology and conservation of owls in the northern hemisphere, Winnipeg, Canada. United States Department of Agriculture, p. 299-307.	N	
II-C 2.4.3.4	Shore RF, Birks JDS, Afsar A, Wienburg CL and Kitchener AC	2003	Spatial and temporal analysis of second-generation anticoagulant rodenticides in polecats (*Mustela putorius*) from their range in Britain, 1992-1999. Environmental Pollution 122: 183-193.	N	
II-C 2.4.3.4	Birks JDS	1998	Secondary rodenticide poisoning risk arising from winter farmyard use by the European Polecat *Mustela putorius*. Biological Conservation 85: 233-240.	N	
II-C 2.4.3.4	Fletcher MR, Hunter K, Barnett EA, and Sharp EA	2002b	Pesticide Poisoning of Animals 2001: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	N	
II-C 2.4.3.4	Fletcher MR, Hunter K, Barnett EA, and Sharp EA	2003	Pesticide Poisoning of Animals 2002: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	N	
II-C 2.4.3.4	Barnett EA, Fletcher MR, Hunter K and Sharp EA	2004	Pesticide Poisoning of Animals 2003: Investigations of Suspected Incidents in the United Kingdom. A Report of the Environmental Panel of the Advisory Committee on Pesticides.	N	
II-C 2.4.3.6	Brakes CR and Smith RH	2005	Exposure of non-target small mammals to rodenticides: short-tem effects, recovery and implications for secondary poisoning. Journal of Applied Ecology 42: 118-128.	N	

Appendix V: Introductory document TMII09 – general and environment

8 May 2009

Revised assessment report on difenacoum based on multiple dossiers from three applicants

Introduction

Finland has been the RMS for difenacoum for which three dossiers were submitted for PT 14. Dossiers were received from Sorex Limited, Hentschke & Sawatzki KG and the Activa/PelGar Brodifacoum and Difenacoum Task Force. Multiple dossiers were also submitted for brodifacoum and bromadiolone for PT 14. According to the guidance for Evaluation of multiple dossiers... (CA-Jun04-Doc.5.6-rev) separate Competent Authority Reports (CARs) shall be prepared for each dossier. After adoption of CARs at the TM, the RMS shall produce a single Assessment Report (AR) of the separate CARs.

The completeness check of dossiers showed that the dossiers of Sorex Limited and Hentschke & Sawatzki KG were complete, whereas the dossier of Activa/PelGar Task Force was incomplete. The last notifier agreed with the Commission that they can resubmit their dossier even though the deadline for submitting dossiers for PT 14 was passed. The resubmitted dossier was accepted as complete in February 2006. It was agreed that evaluation of the complete dossiers should not be postponed until the third dossier is completed.

The evaluation of the complete dossiers started in 2004 and finished in early 2006. The TM discussions on these two dossiers took place in 2006-2007. After adoption of CARs the RMS prepared a single AR which was almost identical to the Doc I of Sorex Limited. The SCB voted difenacoum for Annex I in the end of 2007 based on the dossiers of Sorex Limited and Hentschke & Sawatzki KG. The evaluation of the dossier of the Activa/PelGar Task Force was finished in 2008 and it was handled in a written procedure in the TMs in 2008-2009.

The RMS has prepared an amalgamated AR for difenacoum where data from the Activa/PelGar Task Force has been added to the AR which already covered data from Sorex Limited and Hentschke & Sawatzki KG. This amalgamated AR will exceptionally be discussed at the TM because it is a first time such an AR is prepared. The discussion point is the structure of the AR and the LOEP. This document focuses primarily on the environmental risk assessment and to a lesser extent to physical and chemical properties. The toxicological risk assessment is covered in a separate document.

Structure of the assessment report and the LOEP

The RMS has experienced the requirements of separate CARs and a single AR and LOEP as problematic and welcomes the later versions of the multiple dossier guidance where greater flexibility is allowed for RMS to decide how to compile the CAR for multiple dossier substances. We fail to see the logic behind the separate CARs, when a single AR is required. We would rather merge the data and select the most relevant endpoint values at the evaluation phase. We would also prefer the simultaneous evaluation of dossiers in order to avoid duplicate work.

No detailed guidance is available on how the amalgamation of data from separate dossiers should be done. It is recommended in the latest version of the multiple dossier guidance (CA-May09-Doc.8.3) that data on physical and chemical properties are presented separately and this has been done for difenacoum. Concerning the environmental risk assessment, the evaluation of all three dossiers led to same conclusions even though the individual endpoint values were not identical. After consulting the Commission the RMS added the data from the Activa/PelGar Task Force to the existing AR and hence two endpoint values are given in the LOEP. Consequently, the individual risk assessments done in the separate CARs are reflected in the AR and no effort has been done to re-evaluate the combined data pool. PNECs derived in each CAR and their effects on the conclusions of the risk assessment are given in Table 1.

We would not recommend using the difenacoum AR as a general model for multiple dossier cases. The multiple dossier cases can be different, and hence flexibility and case by case judgement is needed. We would in principle prefer having single endpoint values for one substance and base the risk assessment and LOEP on those values. However, it is not possible to achieve this ideal situation for difenacoum. Re-evaluation of the combined data pool would not be sensible as it would not change the conclusions on the environmental risk. It would neither be economically feasible as we cannot charge on the work done on the amalgamated AR. In addition all work on the AR delays the evaluation of our substances on the 3rd and 4th list.

Proposal of the RMS: The AR and LOEP are accepted in their current form.

Table 1. Effects of different PNECs on the conclusions of the risk assessment in the difenacoum CARs.

PNEC	Sorex	H & S	Activa/ PelGar	Remarks
$PNEC_{water}$ µg/l	0.06	0.06	0.06	$PNEC_{water}$ is based on the lowest fish test result in the Sorex dossier. Agreed at the TMI07 that the most critical data are used for two other applicants.
$PNEC_{sediment}$ mg/kg ww	2.51	2.51	2.51	$PNEC_{sediment}$ calculated with the EPM from the $PNEC_{water}$.
$PNEC_{STP}$ mg/l	2.3	2.43	0.48	Sorex' test was done on *Pseudomonas putida* and EC_{10} value. The test concentration was considered to be close to water solubility. Water solubility of Sorex was 1.7 mg/l at pH 7 and 61 mg/l at pH 9. The required AF is 1. H+S test was done on the activated sludge (OECD 209) and the EC50 of 243 mg/l was determined. The AF 100 was applied. Water solubility of H+S was 0.06 mg/l at pH 7.1 and 1.24 mg/l at pH 9. Setting $PNEC_{STP}$ at the water solubility was not required. Activa/PelGar's test was done on the activated sludge (OECD 209) and the EC50 of > 999.7 mg/l was determined. Setting of $PNEC_{STP}$ at water solubility was required during the written procedure. Water solubility was 0.48 mg/l at pH 6.5 mg/l and 3.7 mg/l at pH 8.9. Difenacoum did not inhibit STP microbes at any concentrations. No risk for the STP microbes was identified in any dossier. Different PNECs do not change the conclusions of the risk assessment.
$PNEC_{soil}$ mg/kg ww	2.04	2.04	0.877	$PNEC_{soil}$ of Sorex and H+S is calculated with the EPM from $PNEC_{water}$. $PNEC_{soil}$ of Activa/PelGar is based on the acute earthworm study and an AF of 1000. Apart from the open area scenario no risk is identified for soil organisms. The use of lower PNEC would remove the risk in the open area scenario, because multiplication by factor 10 is required for the $PEC_{soil}/PNEC_{soil}$ ratio when the $PNEC_{soil}$ is derived with the EPM for substances with log K_{ow} > 5. The different PNECs do not change the conclusions of the risk assessment in three of four scenarios. In one scenario the conclusions would be changed. Data from one applicant cannot be used for the benefit of the other applicant without permission from the first applicant.

PNEC	**Sorex**	**H & S**	**Activa/ PelGar**	**Remarks**
$PNEC_{oral}$ Birds µg/kg food µg/kg bw/day	 3 0.3	 3 0.3	 0.5 0.1	$PNEC_{oral}$ of Sorex and H+S is based on the avian reproduction study of Sorex. An AF of 30 is applied. $PNEC_{oral}$ of Activa/PelGar is based on the avian dietary study and an AF of 3000. Activa/PelGar had also a reproduction study, but due to methodological weaknesses it was not used for the derivation of $PNEC_{oral}$. A high risk for secondary poisoning of birds is identified in all three CARs and the different PNECs do not change the conclusion of the risk assessment. Data from one applicant cannot be used for the benefit of the other applicant without permission from the first applicant.
$PNEC_{oral}$ Mammals µg/kg food µg/kg bw/day	 7 0.3	 7 0.3	 7 0.3	The PNECs are based on identical results from two different tests. $PNEC_{oral}$ of Sorex and H&S is based on Sorex' 90-day rat repeated-dose toxicity test and AF 90. $PNEC_{oral}$ of Activa/PelGar is based on PelGar's 90-day rat repeated-dose toxicity test and AF 90.