Section 7.5.3.1.3 Effects on reproduction of birds
Annex Point IIIA XIII 1.3

Remarks	*2.3 Deviations:* *Exposure was via drinking water and not via food.* *The study is performed on an exposure time of 6 weeks, instead of the 20 weeks required by OECD 206 (version 1984, adopted).* *Ethanol is not envisaged as carrier.* *71.3.2 Deficiencies:* *Control birds were not fed with the carrier (ethanol).* *No information are given on the diet composition.*
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A7_5_3_1_3-1: Method of administration of the test substance

Carrier / Vehicle	Details
Water	De-ionised water
Organic carrier	*Ethanol abs
Concentration of the carrier [% v/v]	0.1, 0.2, 0.3 and 0.4 µg/ml
Other vehicle	None
Function of the carrier / vehicle	Solvent for test material

*In this study the control birds were treated with the vehicle of water only. The test item was dissolved in ethanol because it is not sufficiently soluble in water. The highest concentration of ethanol in any group was 4 mL/L (0.4% v/v). In other similar studies performed in this laboratory, the same species of quail have been given water with low levels of ethanol; in these studies there were no symptoms or mortality in the control animals during 6 weeks. The results were not significantly different to birds given only water. In many toxicology and ecotoxicology studies performed with the full range of anticoagulants in this laboratory and many other laboratories, ethanol has been used because:
- it is one of the few suitable solvents for this class of chemistry,- it is non-toxic and is readily metabolised by birds and mammals at the levels used.It is true that high levels of ethanol can interfere with warfarin metabolism. However, no metabolites of warfarin are common to this test item (or to any modern coumarin anti-coagulants), the metabolic pathways are not the same. Also, the protein binding of warfarin is completely different to that of modern anti-coagulants so no comparisons can be made regarding effects of ethanol. There is no indication that low levels of ethanol could

interfere with this test item. It is considered that there is no realistic risk that ethanol could have had a significant effect on the test item effects in this study. It should be noted that the warfarin data indicates that high ethanol intake can potentiate the risk of toxicity. This would suggest that in the very unlikely event of an interference, the test system would be more sensitive and would hence give a more conservative safety evaluation. Only the opposite would be of any regulatory concern.

Table A7_5_3_1_3-2: Test animals (if more than one species is used, for each species one table)

Criteria	Details
Species/strain	Japanese quail (Coturnix coturnix japonica)
Source	Dezso Rokolya quail breeder, Csavoly, Szent Itvan u. 83, H-6448, Hungary
Age (in weeks), sex and initial body weight (bw)	9 weeks old a the initiation of the test. 48 males and 96 females BW Range- males 177-220g BW Range- female 170-296g
Age range within the test	See above
Breeding population	Not stated in report
Amount of food	Mean ranged from 33.08 and 26.44 g/animal/day for the control group.
Age at time of first dosing	9 weeks old
Health condition / medication	All animals were reported to be in good health.
Pre-treatment	None

Table A7_5_3_1_3-3: Test system

Criteria	Details
Test location	Holding pens
Holding pens	Each pen has floor space that measured approximately 50cm x 50cm. Ceiling height is 40 cm. External walls, ceiling and floors are constructed of galvanised wire
Number of animals (male/female)	144 (48 males and 40 females)
Number of animals per pen [cm²/bird]	One male and one female in each pen
Number of animals per dose	36 birds per does
Pre-treatment / acclimation	Not stated in the report
Diet during test	Not stated in the report
Dosage levels (of test substance)	0, 17.5, 35.0, 70.0 µg/kg
Replicate/dosage level	*If appropriate, include data (e.g. 3 replicates/dosing level)*
Dosing method	Mixed with drinking water

Criteria	Details
Dosing volume per application	Concentration in drinking water was 0, 0.1, 0.2 and 0.3 (0.4 from the second week) µg/ml
Frequency, duration and method of animal monitoring after dosing	A record of all mortality, signs of toxicity, or abnormal behaviour were recorded on a daily basis. Body weight measurements in adults were made at the start of the acclimatisation period and the end of the exposure period. Body weight measurements were made on hatchlings at the end of the rearing period. Feed consumption was determined in adults at one-week intervals throughout the study. Average feed consumption was determined for hatchling in the period of days 1-7 and days 8-14 after hatching. Gross necropsy was performed on adult birds after mortality or at termination of the study. Organ weight for all adult birds were measured at the termination of the test.
Time and intervals of body weight determination	See above
Incubation, storing and hatching	Eggs were stored not more than 7 days at the temperature of 10-16°C and 55-75% relative humidity. The eggs were incubated at 37.4-37.7°C. Relative hymidity was 50-70%. Eggs were transferred to hatcher on day 14. Temperature in the hatcher was 37.0-37.6°C relative humidity was 70-75%. Hatching was completed on day 18.
Test period after egg-laying	The study was continued for 14 days after the eggs hatched.
Turning of eggs	Device for turning eggs was automatic as well.

Criteria	Details
Collection period for eggs	The eggs were collected in a 7-day period.

Table A7_5_3_1_3-4: Test conditions (housing)

Criteria	Details
Test temperature	Recorded twice daily
Shielding of the animals	Not stated in the report
Ventilation	Ventilated with HELISO-HS type ventilator, maximal aeration 18 times/hour.
Relative humidity	Recorded twice daily
Photoperiod and lighting	Photoperiod was 7-8 hours per day at the beginning of acclimation/stabilisation then during the two weeks it was continuously increased to 16-18 hours per day.
Storing, incubation and hatching conditions for eggs	See above table
Environmental conditions for young birds	Birds were kept indoors in covered brooder pens, separated by dose levels. Each pen had floor space that measures 1.5 X 1.0m. Ceiling height is 40cm. External walls, ceiling and floors are constructed of galvanised wire. Temperature was 30°C-38°C.

Table A7_5_3_1_3-5: Values of reproduction ability

Parameter	Test substance dosage level (mg/kg bw)	Week of Expostion/No of EggsWeek					
		1	2	3	4	5	6
Egg production (number of eggs laid per hen)	Control	5.8	5.6	5.5	5.1	5.3	4.2
	17.5 µg/kg	6.0	5.7	6.0	5.5	5.6	5.2
	35.0 µg/kg	5.7	5.0	5.6	6.2	4.3	5.8
	70 µg/kg	5.5	7.3	4.9	6.7	5.6	7.6
Percentage of cracked eggs		Percentage of the broken eggs of eggs laid prior to exposure			Percentage of the broken eggs of eggs laid		
	Control	0.67			6.74		
	17.5 µg/kg	1.87			4.98		
	35.0 µg/kg	0.74			6.13		
	70 µg/kg	1.05			5.85		
Viability (per cent viable embryos of eggs set)							
Hatchability (per cent hatching of eggs set)							
Percentage of hatchings that survive to 14 days	Control	73.6	70.2	48.2	71.7	51.1	66.7
	17.5 µg/kg	73.0	58.6	67.7	70.7	52.0	80.1
	35.0 µg/kg	89.4	82.0	69.9	92.5	78.9	96.0
	70 µg/kg	96.6	68.9	89.2	94.1	100.0	100.0
Number of 14-day old survivors per hen							
Eggshell thickness (mm)	When compared to the control the mean eggshell thickness was significantly different only in one case in the group of 17.5µg/kg bw on the first week of pre-treatment. No test item related effect was observed during the exposition period.						

Table A7_5_3_1_3-6: Validity criteria for bird reproduction test according to OECD 206

	Fulfilled	Not fulfilled
Mortality of control animals <10%	X	
Average number of 14-day-old survivors per hen in controls ≥ 14, 12 and 24 for mallard duck, bobwhite quail and Japanese quail	X	
Average eggshell thickness for the control group ≥ 0.34, 0.19 and 0.19 mm for mallard duck, bobwhite quail and Japanese quail	X	
Concentration of the test substance in the diet ≥ 80 % of the nominal concentration throughout the test period		X

Section A7.5.4.1 Annex Point IIIA XIII 3.1	Acute toxicity to honeybees and other beneficial arthropods, for example predators	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible** [ ] **Scientifically unjustified** [ ]	
Limited exposure [ ]	**Other justification** [ ]	
Detailed justification:	Compound is of very low water solubility and is not used in situations where bees or beneficial arthropods are exposed. It is used in highly localised and limited areas such as sewers where bees and beneficial arthropods do not exist, and it is not applied in a widespread fashion to extensive areas where leaching and run-off which might contaminate their habitat is possible. It is of low vapour pressure and is not applied as a spray or vapour which might contaminate their environment. Many years of use in a wide range of situations has shown no effect on bees or beneficial arthropods. Plants are not treated with rodenticides.	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*November 2006*	
Evaluation of applicant's justification	*Accepted*	
Conclusion	*No need to submit a study*	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A7.5.5 Annex Point IIA VII 7.5	Bioconcentration, terrestrial	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [X] **Limited exposure [X]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	The TNsG on data requirement ask for at least the physical-chemical properties of the active, which are relevant for possible bioconcentration. A new log Pow is to be obtained at SafePharm Laboratories and will be available in September 2006 (see copy of contract of phys-chem studies). However for now the value of 8.5 (pesticide manual 13th edition) will be used for the purposes of estimating the BCF. Using the parabolic equation (no. 75) in the TGD (part II) : Log BCFfish = -0.20 * $logKow^2$ + 2.74 * logKow - 4.72 (eq. 75) Log BCFfish = -0.20 * 8.5^2 + 2.74 * 8.5 – 4.72 = 4.12 BCF fish = 13183 This is indicative of high potential to bioconcentrate. In addition the BCF for earthworm has also been calculated as 3.79E+06 $l/kg_{wetearthworm}$ (TGD part II, 2003 eq. 82d, see doc IIB). The TGD does state however that the model used worked well for earthworms kept in water , but for soil exposure the experimental BCFs were somewhat lower than the predictions by the model. There is however an indication that bioconcentration could occur in earthworms due to the high value obtained and also because it is well known that second-generation rodenticides accumulate in living organisms. So, both the Log Pow, and calculate BCFs indicate bioconcentration in terrestrial organisms is likely. In the risk assessment (IIB/C) it is apparent that a high risk of secondary poisoning to non-target organisms does exist, with PECoral, predator/PNEC ratios well above 1. On the basis that it is acknowledged above that bioconcentration in terrestrial organisms can occur, if given long-term exposure to the active, a derogation to perform a bioconcentration study is requested. Please also note that a refinement to both the log Pow and BCFs can be carried out once a reliable value is obtained in the SafePharm study. It is however not expected to change the justification for not performing a study.	X
Undertaking of intended		

Section A7.5.5 Annex Point IIA VII 7.5	Bioconcentration, terrestrial
data submission [ ]	
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*December 2006*
Evaluation of applicant's justification	*Based on the new experimentally derived Pow (8.35E4) available, the $BCF_{earthworm}$ is re-calculated according to TGD (eq. 82d) as follows:* *$BCF_{earthworm} = (0.84+0.012Kow)/RHO_{earthworm}$* *$BCF_{earthworm} = (0.84+0.012* 8.35E4)/1 = 999$*
Conclusion	*$BCF_{earthworm}$ is estimated from the experimental Kow to be 999.* *No need to provide a study on the bioconcentration terrestrial.*
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.5.5.1 Annex Point IIA VII 7.5	Bioconcentration, further studies	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [X]**	**Technically not feasible [ ]** **Scientifically unjustified []** **Other justification [X]**	
Detailed justification:	The risk assessment for PEC/PNEC in birds eating earthworms exposed to brodifacoum, indicates a PEC/PNEC of 103217 (see IIC). The PEC is derived from the ESD (2003). The PNEC is derived from a study (see Doc IIIA) and the TGD (pt II) provided the conversion and assessment factors. It is believed that the calculation for BCF in earthworms already indicates that bioconcentration is likely to occur and that if birds eat earthworms which have bioaccumulated brodifacoum, they are at risk of dying. Also, the use of the product is limited to areas such as sewers, where birds are absent and in and around buildings. Brodifacoum will be excreted by rats in a fairly confined area around the building although the main exposure to the soil is expected to be from spills during application, refilling and disposal operations(ESD,2003). Rats could also excrete further afield, although the expected concentrations would be a lot less than those calculated from the ESD, which are based on a relatively confined zone of 10metres around the building (farmhouse in the ESD). Based on the limited areas that would be a risk to earthworm-eating birds, around buildings such as farmhouses, together with the risk assessment PEC/PNEC >1 for birds eating earthworms near to buildings with bait, it is believed that a study would not change anything we already know – which is that there is a high risk of secondary poisoning of birds from eating earthworms near to buildings treated with bait - and therefore a derogation to perform a bioconcentration in earthworms is requested.	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*November 2006*	

Section A7.5.5.1 Annex Point IIA VII 7.5	Bioconcentration, further studies
Evaluation of applicant's justification	*Accepted*
Conclusion	*No need of further study on bioconcentration*
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.5.6 Annex Point IIIA XIII 3	Effects on other terrestrial non-target organisms	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [X]	**Other justification [ ]**	
Detailed justification:	The risk assessment has identified a high risk of secondary poisoning from predation of poisoned rats. However this assumes that poisoned rats are widely eaten. The use of the rodenticide in sewers is not an issue since predators don't inhabit that environment. So the remaining risk is to predators eating rats in and around farm buildings. It is not applied in a widespread fashion to extensive areas. Many years of use in a wide range of situations has shown only limited effects on terrestrial non-target organisms provided product is used correctly. It is also believed that since a high risk of primary and secondary poisoning has already been identified it is more important to consider further ways to ensure that non-target predators do not have access to bait stations and that any bait removed from the station by rats, and rat carcasses are prudently removed. This could be reflected with perhaps more stringent labelling. On the above grounds, a derogation to perform further tests is requested.	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*November 2006*	
Evaluation of applicant's justification	*Accepted*	
Conclusion	*No need of further studies on terrestrial non target organisms*	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A7.5.7.1.1 Effects on mammals - Acute oral toxicity

Annex Point *IIIA XIII.1.1* *Rabbit poisoning trials - Brodifacoum residues*

Official use only

		72 REFERENCE
72.1	**Reference**	C.G. Rammell, J.J.L. Hoogenboom, M. Cotter, J.M. Williams and J. Bell (1984) Brodifacoum residues in target and non-target animals following rabbit poisoning trials. New Zealand Journal of Experimental Agriculture, 1984, Vol. 12: 107-111.
72.2	**Data protection**	No, published paper.
72.2.1	Data owner	© Crown copyright 1984
72.2.2	Criteria for data protection	No data protection claimed
		73 GUIDELINES AND QUALITY ASSURANCE
73.1	**Guideline study**	The guideline study is not stated in the published paper.
73.2	**GLP**	The GLP status of the study is not stated in the published paper
73.3	**Deviations**	No
		74 MATERIALS AND METHODS
74.1	**Test material**	Brodifacoum
74.1.1	Lot/Batch number	Batch numbers not stated in the published paper.
74.1.2	Specification	Not stated in the published paper
74.1.3	Description	
74.1.4	Purity	94%
74.1.5	Stability	A specific statement on stability is not provided within the paper.
74.1.6	Radio labelling	
74.2	**Test Animals**	
74.2.1	Species	Target animals – rabbits
74.2.2	Strain	Not stated in the published paper
74.2.3	Source	Wild
74.2.4	Sex	Male and female
74.2.5	Age/weight at study initiation	All ages and weights
74.2.6	Number of animals per group	Not applicable as this is a trial in open countryside
74.2.7	Control	No

Section A7.5.7.1.1 **Effects on mammals - Acute oral toxicity**
Annex Point *IIIA XIII.1.1* *Rabbit poisoning trials - Brodifacoum residues*

	animals	
74.3	**Administration/ Exposure**	Oral
74.3.1	Preparation of test site	Not applicable
74.3.2	Concentration of test substance	Final estimated concentration in the baits of 50 mg/kg.
74.3.3	Specific activity of test substance	Low density, cereal based 'Mapua' baits sprayed with a water/monopropylene glycol suspension (4/1, v/v) of technical brodifacoum (94%)
74.3.4	Volume applied	1500-4000 baits/ha (Each bait 0.83 g) laid at 3 sites
74.3.5	Sampling time	Dead rabbits and other non-target animals were collected 4-28 days after baits were laid.
74.3.6	Samples	Liver, muscle and fat tissues taken for analysis..

75 RESULTS AND DISCUSSION

75.1 Result of study

Animals, in which brodifacoum was detected, showed haemorrhages at necropsy typical of anticoagulant poisoning.

Haemorrhage sites in rabbits were massive abdominal (52%), thoracic (17%) and the remaining (31%) were muscle, caecum, stomach, kidney, mesentery and placenta of pregnant does.

Levels of brodifacoum >0.05mg/kg was detected in 41 out of 43 dead rabbits analysed and in all 14 other animals found dead in the experimental areas. High levels of brodifacoum were found in the liver, up to 11.7 mg/kg, and up to 2.1 mg/kg in fatty tissues. The mean liver level for females was 5.8 mg/kg compared to 3.2 mg/kg for males.

Other dead animals found were, hare, sheep, cat, paradise duck, seagull, hawk, magpie and passerine, all having significant levels of brodifacoum in the liver.

76 APPLICANT'S SUMMARY AND CONCLUSION

76.1 Materials and methods

76.2 Results and discussion

The higher levels of brodifacoum in the liver of females may bedue to the fact that the trial was during the breeding season as 21% of females autopsied were pregnant. This means that the males would have been more active than female due to territorial displays, chasing and fighting. This in turn would increase the effect of the coagulant poison. The earlier death of the males would then account for the lower levels of brodifacoum in their liver.

The published LD_{50} for cats is 25 mg/kg, ferrets is approx 9.2 mg/kg and hawks approx 10 mg/kg. For typical weights of 750g for the hawk and 3.25 kg for the cat this would give LD_{50} values of 7 mg and 80 mg. To get this dose would require them to have consumed about 175 and 2000 baits respectively. As there are predominantly carnivores this seems to

Section A7.5.7.1.1 Effects on mammals - Acute oral toxicity

Annex Point *IIIA XIII.1.1* *Rabbit poisoning trials - Brodifacoum residues*

	be unlikely therefore the dose must have come from poisoned rabbit carcasses.	
76.3 Conclusion	Brodifacoum is an effective coagulant poison for the control of rabbits. The presence of brodifacoum in the carcasses of poisoned rabbits poses hazards to rabbit predators. Although the predators do not control dense populations of rabbits they do help in some areas. It is therefore desirable that poisoning operations have minimal impact on rabbit predators. To help reduce the effect on non-target animals it may be necessary to reduce the toxicity of the bait in order to reduce the residue levels.	
76.3.1 Reliability	1	X
76.3.2 Deficiencies	No	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*November 2006*
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	*-2/4 .* *The study is not acceptable as acute toxicity test as such, because it does not follow any guideline and the results cannot be used for risk assessment. Rather, the study provides useful information on the risk of primary poisoning of non target vertebrate in the field.*
Acceptability	
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A7.5.7.1.2 Annex Point IIIA XIII 3.4	Effects on mammals - Short term toxicity	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [X]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	The compound belongs to a well-known and closely analogous group of anticoagulants with very similar properties. All studies on vertebrates show the same effects, primarily loss of blood coagulation, and these are shown clearly in acute studies. There is little species differentiation in effects or dose response, and there are no positive findings in genotox studies. To avoid acute effects, doses in repeat dose studies must be kept very low, and the potential for exposure to rodenticides is limited by the nature of their use. A second species 90-day feeding study is therefore considered unjustified.	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*November 2006*	
Evaluation of applicant's justification	*Accepted*	
Conclusion	*No need of the study.*	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A7.5.7.1.3 Annex Point IIIA XIII 3.4	Effects on mammals - Effects on reproduction	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [ ]**	
Limited exposure [ ]	**Other justification [X]**	
Detailed justification:	A 2-generation study has been performed on the rat. (see section 6.8)	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*November 2006*	
Evaluation of applicant's justification	*Accepted*	
Conclusion	*No need of the study.*	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A7.6 Annex Point IIA VII 7.8 — Summary of ecotoxicological effects and fate and behavious in the environment

Official use only: X

The active substance is a large aromatic organic compound of low volatility with two polar groups, which can potentially ionise at environmental pH. The active substance has a high Log Pow (> 4), a high predicted BCF of 568.9, is not readily biodegradable and is of low solubility (<0.1 mg/l). The predicted Log Koc indicates that the active substance would not be mobile in soil and would be expected to absorb to soil particles. The substance does not undergo hydrolysis (t½ > 1 year). It is however predicted undergo rapid indirect photolysis with OH radicals and ozone (t½ = approximately 2 hours) and undergoes rapid direct photodegradation (t½ = 0.217 days). There are no predicted effects on the atmosphere.

The active substance is very toxic to aquatic organisms (E/LC_{50} < 1 mg/l) and is potentially bioaccumulative (log Kow >3)

Determination of PNEC's

PNEC for aquatic organisms

On the basis of acute toxicity data for fish, invertebrates and algae and a chronic NOEC for algae only, the PNEC is derived from the lowest L/EC_{50} value (fish 96h LC_{50} = 0.042 mg/l, algae 72h E_rC_{50} = 0.04 mg/l),) with a safety factor of 1000. Therefore,

PNEC aquatic organisms = 4.0E-05 mg/l

PNEC for the sediment-dwelling organisms

For the sediment compartment a quantitative risk characterization cannot be carried out, therefore the risk for this compartment is covered by the risk for the aquatic compartment.

PNEC for STP micro-organisms

An EC_{10} for *Brodifacoum* is derived from a respiration inhibition test, where no effect on sewage treatment processes was observed at a nominal concentration much higher than its water solubility. Therefore the EC_{10} was set as > 0.058 mg/l (WS at pH=7, 20°C) and the PNEC was derived by applying an AF=10.

PNEC STP micro-organisms = >0.0058 mg/l.

PNEC for terrestrial organisms

The PNEC for terrestrial organisms is calculated from the 14d LC_{50} > 879.6 mg/kg wwt soil, obtained from a study with earthworms, and applying an AF 1000:
$PNEC_{soil}$ = >0.88 mg/kg wwt soil

PNEC for birds

The long-term avian toxicity endpoints for *Brodifacoum* were obtained from read across to reproduction toxicity of Difenacoum. According to TGD, PNECs are derived by applying an AF of 30 to the NOECs as follows:
$PNEC_{oral\text{-}birds}$ = 0.012 mg *Brodifacoum* /kg diet / 30 = 0.0004 mg *Brodifacoum* /kg diet
$PNEC_{oral\text{-}birds}$ = 0.0012 mg *Brodifacoum* /kg bw/d / **30** = 0.00004 mg *Brodifacoum* /kg bw/d

PNEC for mammals

The lowest mammalian NOAEL (0.001mg/kg bw/day) comes from a two-generation fertility study with rats and refers to parent females. This endpoint was converted to NOEC $_{mammal,food}$ =0.02 mg/kg food. As the exposure lasted 90 days as a minimum, for PNEC derivation an AF_{oral} of 90 is applied:

$PNEC_{oral\text{-}mammals}$ = 0.02/90 = 2.22E-04 mg/kg food, corresponding to

Section A7.6 Summary of ecotoxicological effects and fate and behavious in the environment
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$PNEC_{oral\text{-}mammals}$ = 0.001 mg/kg bw day/90 = 1.1 E-05 mg/kg bw.

Metabolites

No degradation or transformation products of Brodifacoum in water were detected in water. No significant metabolites are expected to be formed in soil or introduced in soil via urine or foeces of contaminated rats.

Section IIIA.8 Annex Point IIA. VIII	Measures necessary to protect man, animals and the environment	Official use only
8.1 Recommended methods and precautions concerning handling, use, storage, transport or fire (IIA, VIII.8.1)	Handling: Product must be handled in a safe manner. Use Concentrate for producing ready for use anti-coagulant rodenticide Storage: Store in original container under cool and dry conditions in a secure (lockable), well ventilated place, inaccessible to children and away from foodstuffs, animal feedstuffs and products which may have an odour Transport: Hazard classification for transport: TOXIC, MARINE POLLUTANT UN-No Coumarin derivative pesticide, solid, toxic, n.o.s (BRODIFACOUM) Class 6.1 Hazard ID 66 Proper Shipping name Coumarin derivative pesticide, solid, toxic (contains difenacoum) UN-No 3027 Packing Group 1 Class 6.1 Fire:Suitable Extinguishing Media Keep fire exposed containers cool by spraying with water if exposed to fire. Fight surrounding fire with foam, water fog, or dry powder. DO NOT USE WATER JETS Special protective equipment for fire-fighters In the event of fire, wear self contained breathing apparatus, a chemical protection suit, suitable gloves and boots.	
8.2 In case of fire, nature of reaction products, combustion gases, etc (IIA, VIII.8.2)	This product is not flammable but is combustible. Avoid run-off into water courses. Self-contained breathing apparatus should be won by fire-fighting personnel.	
8.3 Emergency measures in case of an accident (IIA, VIII.8.3)	Skin contact Obtain medical advice immediately. Remove contaminated clothing. After contact with skin, wash immediately with plenty of water, followed by soap and water in order to minimise skin contact. Eye contact Obtain medical advice immediately. Irrigate eyes with copious amounts of water. Inhalation Remove person to fresh air. Obtain medical advice immediately. Ingestion Do no induce vomiting. If swallowed, obtain medical advise immediately. Wash out mouth with water. Guide to the doctor Brodifacoum is an indirect anit-coagulant. Vitamin K1 is antidotal. In the case of suspected poisoning, determine prothrombin times not less	

Section IIIA.8 Annex Point IIA. VIII	Measures necessary to protect man, animals and the environment	Official use only
	than 18 hours after consumption. If elevated, administer vitamin K1 and continue until prothrombin times normalise. Continue determination of prothrombin time for three days after withdrawal of antidote and resume reatment if elevation recurs in that time.	
8.4 Possibility of destruction or decontamination following release in or on the following: (IIA, VIII.8.4)		
a. air	Brodifacoum has a low vapour pressure, therefore the potential for evaporation is low The vapour pressure is 5×10^{-5} Pa. As a rodenticide, this material is not intentionally aerosolised. Therefore, destruction in air is not a concern.	
b. water, including drinking water	Prevent further leakage or spillage if safe to do so. Prevent entry into watercourses, sewers.	
c. soil	Direct and/or intentional release to soil is not anticipated for the use of the product as a rodenticide. In the event of a significant accidental release, inform the appropriate authority.	
8.5 Procedures for waste management of the active substance for industry or professional users (IIA, VIII.8.5)	The best means of disposal of any product is through proper use according to the label. For the product incinerate under controlled conditions. For the pack, do not dispose of the pack in domestic refuse. Empty completely, puncture or crush and dispose of safely to Local Authority and National requirements.	
8.5.1 Possibility of re-use or recycling (IIA, VIII.8.5.1)	Where possible recycling is preferred to disposal or incineration.	
8.5.2 Possibility of neutralisation of effects (IIA, VIII.8.5.2)	Incineration is recommended.	
8.5.3 Conditions for controlled discharge including leachate qualities on disposal (IIA, VIII.8.5.3)	None	
8.5.4 Conditions for controlled incineration (IIA, VIII.8.5.4)	Must be incinerated in a suitable incineration plant holding a permit delivered by the competent authorities.	
8.6 Observations on undesirable or unintended side-effects (IIA, VIII.8.6)	None	
8.7 Identification of any substances falling within the scope of List I or List II of the Annex to Directive	None	

Section IIIA.8 Annex Point IIA. VIII	Measures necessary to protect man, animals and the environment	Official use only
80/68/EEC (IIIA, VIII.1)		

Section A 8 Annex Point IIA VIII.8.1 to VIII.8.6 and IIIA VIII.1	Measures necessary to protect man, animals and the environment	

Evaluation by Competent Authorities

	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*April 2007*
Materials and Methods	Applicants version is acceptable
Results and discussion	Adopt applicant's version
Conclusion	Applicants version is acceptable
Reliability	
Acceptability	Acceptable
Remarks	

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section IIIA.9 Annex Point IIA. IX	Classification and Labelling	Of use
9.1 Classification	T+: Highly toxic	
9.2 Proposed Labelling	R-phrases: R27/28: Very toxic in contact with skin and if swallowed R48/24/25: Toxic: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed S-phrases: S36/37: Wear suitable protective clothing and gloves. S45: In case of accident or if you feel unwell, seek medical advice immediately (show label where possible)	
9.3 Existing Classification and labelling (Annex I of Directive 67/548/EEC)	Brodifacoum is listed on Annex 1 of 67/548/EEC is classified as T+, N 27/28, 48/24/25, 50/53	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	

EVALUATION BY RAPPORTEUR MEMBER STATE

Date June 2007

Section IIIA.9 Annex Point IIA. IX	Classification and Labelling	Of use

Remarks

On basis of study results classification of brodifacoum is proposed according to principles detailed in Ann Council Directive 67/548/EEC (with amendments and adaptations).
The proposed classification for environment was agreed in April 2006 by the Technical Committee on Clas and Labelling (TC C&L) of Dangerous Substances.

The classification for human health effects is in May 2007 still under discussion. A provisional classification was decided in November 2006 by the TC C&L, but without a final decision on the category to be used (Repr Repr.Cat 2). The proposed classification for brodifacoum for acute and repeated dose toxicity was agreed upon 2007 the provisionally classification for reprotoxicity was not confirmed as the TC C&L decided to awa results from studies on anticoagulant rodenticides before finalising the discussion on reprotoxicity. concentration limits for brodifacoum were agreed upon as proposed.

Risk phrases	R26/27/28, R43, R48/23/24/25, R50/53, [R61]
Safety phrases	S20/21, S36/37, S35, S36/37, S45, S60, S61 (S1/2 is not required as the substance is never available to the public.)
Proposal for labelling	as in Directive 67/548/EEC, 99/45/EC and on the basis of data and pragmatism: T+; R26/27/28, R43, R48/23/24/25, N; R50/53, [R61]
Existing classification and labelling	as in Directive 67/548/EEC: T+;R27/28, T;R48/24/25, N;R50/53 (S1/2), S36/37, S45, S60, S61
Specific concentration limits for the environmental classification	C ≥ 2.5% T+, N; R26/27/28-48/23/24/25-43-61-50/53 1% ≤ C <2.5% T+, N; R26/27/28-48/23/24/25-43-61-51/53 0.5% ≤ C< 1% 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

Classification and proposed labelling based on Regulation EC 1272/2008

with regard to physical/chemical data	None
with regard to Health Hazard	Acute Tox 2 H300 Acute Tox 1 H310 Acute Tox 1 H330 STOT RE 1 H372 Repr. 1B H360D* Skin Sens 1 H317
with regard to Environment	Aquatic acute 1 H400 Aquatic chronic 1 H410
Signal Word	Danger
Symbol	GHS06, GHS08, GHS07,GHS09
Hazard statement codes	**H300: Fatal if swallowed** **H310: Fatal in contact with skin**

Section IIIA.9 Annex Point IIA. IX	Classification and Labelling	Of use
	COMMENTS FROM ...	
Date	*Give date of comments submitted*	
Remarks		