Doc IIIA/Section 7.5.6 Field trial used to assess the risks to non-target organisms.

BPD Data Set IIIA/Annex Point XIII.3

1.4 Application of test substance

Criteria	Details
Application procedure	Rodent presence was determined by using tracking patches and census baiting. Track scores were recorded for three days pre-treatment and three days post-treatment as a means of population census. At 15/25 sites the bait was weighed at placement and conclusion of the treatment period. On the remaining 10 sites visual assessments of bait consumption were carried out. All the baits were placed according to the Experimental Use Permit (10182-EUP-20). The type of bait station (rat or mouse) used on each site was determined by the results of the pre-treatment survey. Radio-tracking of owls was carried out every 2 to 3 days initially, but once most transmitters had been fitted to the owls, location of owls was attempted daily during roosting and feeding periods, especially after the rodenticide treatment. Owls with mortality transmitters only had to be heard to determine the status, dead or alive. Owls with regular transmitters were frequently 'walked out' and visually observed to determine their status and location.
Delivery method	Amounts of Talon Pellets were placed in appropriate bait stations (rat or mouse) and located in protected situations.
Dosage rate	Not stated
Carrier	None
Concentration of liquid carrier	Not applicable
Liquid carrier control	Not applicable
Other procedures	Radiotelemetry was used to determine if radio-equipped owls used treated farms for roosting or feeding, as well as the potential to recover any mortalities.

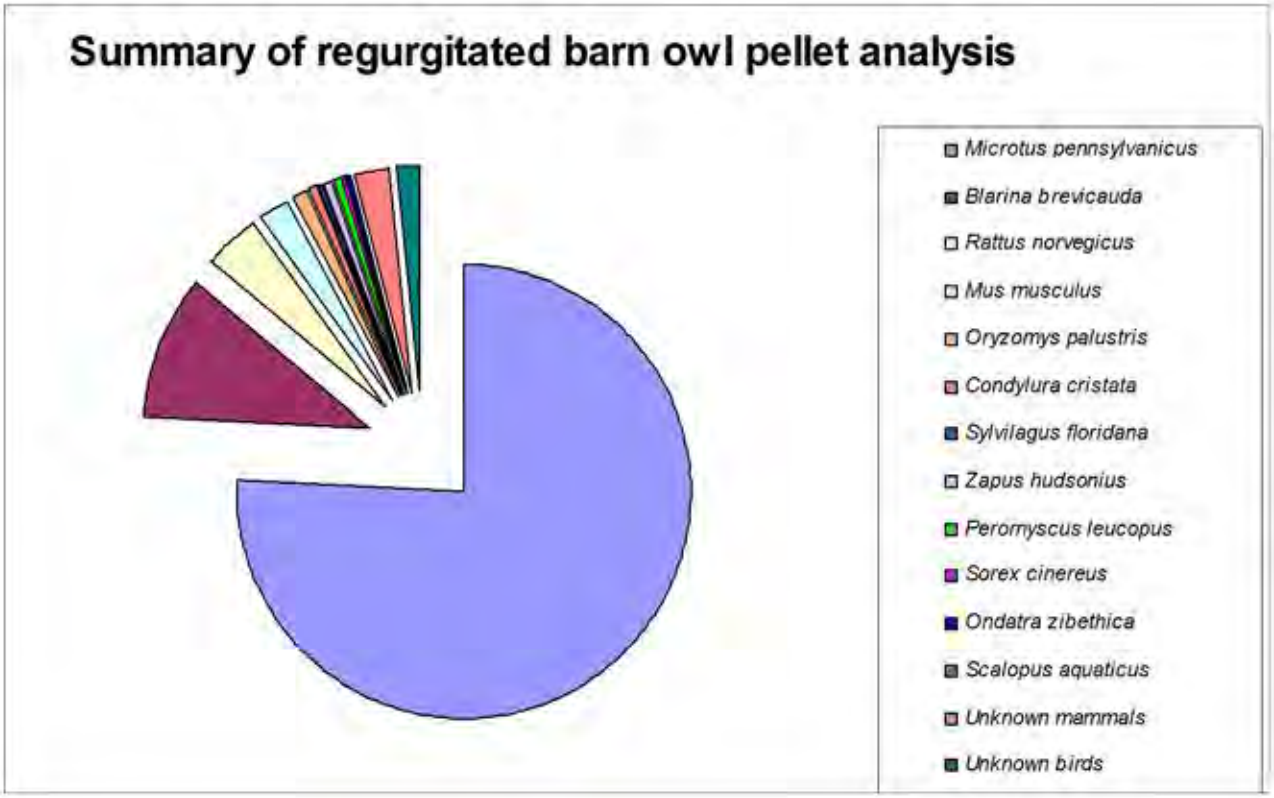
Doc IIIA/Section 7.5.6 Field trial used to assess the risks to non-target organisms.

BPD Data Set IIIA/Annex Point XIII.3

1.5 Test conditions

Criteria	Details
Substrate	Not applicable
Incubation temperature	Not applicable
Moisture	Not applicable
Aeration	Not applicable
Method of exposure	The bait is laid in bait stations in appropriate locations and the rats or mice come across the bait during their normal foraging periods. The sites chosen had barn owls present in either roosting or nesting sites. If the owls also fed on these sites then the owls could be exposed to rats or mice that had consumed the Talon Pellets during the treatment period.
Ageing of samples	Fresh samples of Talon Pellets were used.
Other conditions	None

IIIB 7_7_7_1 – 1 Chart of Owl Pellet Analysis.



Doc IIIA/Section 7.5.7(1)

BPD Data Set IIIA/Annex Point XIII.3.4

Effects on mammals

Secondary toxicity of brodifacoum to dogs.

Official use only

1 REFERENCE

1.1 Reference [redacted], 1978. Talon: Secondary toxicity of brodifacoum to dogs (Beagles), (North Carolina). ICI Americas Inc. Report Series TMUD1997/B (unpublished) [redacted]

1.2 Data protection [redacted]

1.2.1 Data owner [redacted]

1.2.2 Companies with Letter of Access [redacted]

1.2.3 Criteria for data protection [redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study No guideline was stated in the report. The study was conducted in accordance with accepted scientific principles of the time.

2.2 GLP No, the study pre-dates the requirements of GLP.

2.3 Deviations No

3 MATERIALS AND METHODS

3.1	**Test material**	A brodifacoum solution in polyethylene glycol 300 at a dose of 1.5mg/ml (15mg of brodifacoum per kg of rat) to simulate feeding on 50ppm Talon Pellets.	
3.1.1	Lot/Batch number	Not available	X
3.1.2	Specification	Not stated	X
3.1.3	Purity	Not stated	X
3.1.4	Further relevant properties	The test material was administered to simulate rats feeding on Talon Pellets which contain a nominal concentration of 50ppm brodifacoum. The amount administered would give each rodent a dose of 15mg of brodifacoum per kg of rat, presenting a worst-case situation and simulating feeding on 50ppm Talon Pellets until death. At death, each animal was sliced into 2 sections and ground into a 'rat meal' using a conventional electric meat grinder. Individual packs were prepared and frozen. Control rats were prepared in a similar manner except that no brodifacoum was administered. Diet was thawed for 14-16 hours before being presented to the dogs.	
3.1.5	Radiolabelling	The test material was not radiolabelled.	
3.1.6	Method of analysis	None	
3.2	**Reference substance**	No	
3.2.1	Method of analysis for reference substance		
3.3	**Testing/estimation procedure**		
3.3.1	Test system/ performance	Dogs were selected to present a realistic model of what would be expected if a domestic dog were allowed to consume rats intoxicated with brodifacoum. Each dog was decontaminated on arrival at the laboratory and blood samples were taken to determine the health status of the animals. 3 groups of dogs, one male and one female, were used. The groups were allocated to 1, 3 and 4 day no-choice feeding studies. One male control animal was also used. Each animal was provided with 650g of rat meal on each day for the period of the test. 650g or 75% of the usual daily consumption was used to ensure complete consumption and also to reflect that dogs would not be expected to have an unlimited supply of rats. Following treatment, the animals were observed for 10 days and any signs were recorded. Post-mortem was carried out on all animals.	
3.3.2	Estimation of bioconcentration	Bioconcentration was not measured. The study was performed to investigate the potential for secondary toxicity to dogs if they consume rodents after the rodents have consumed a product containing the active substance, brodifacoum.	

4 RESULTS

4.1 Experimental data

4.1.1 Mortality/behaviour

One dog died after consuming 1177.1g of 'rat meal' which would have provided a theoretical dose of 1.85mg/kg of brodifacoum. The pre-test blood sample indicated that this animal was slightly anaemic which may partially explain why another animal consumed 1950.0g of 'rat meal' which provided a theoretical dose of 2.22mg/kg and survived.

4.1.2 Food consumption

All consumption data was recorded and theoretical maximum doses of brodifacoum were calculated. These calculated theoretical doses do not allow for detoxification or excretion of brodifacoum or its metabolic products in the rat.

Amount of rats consumed, g and dose of brodifacoum ingested, mg/kg by dogs.

Group, no choice, day	Animal	Bodyweight, kg	Total rat meal consumption, g	Brodifacoum dose ingested, mg/kg	Mortality, days
1 day	1M	10.20	650.0	0.96	-
1 day	2F	6.35	650.0	1.54	-
3 day	3M	13.15	1950.0	2.22	-
3 day	4F	6.23	757.5	1.82	-
4 day	5F	8.16	142.4	0.26	-
4 day	6M	9.52	1177.1	1.85	9
Control	7M	8.72	0	0	-

4.1.3 Results in graphical format

Refer Figure A7_4_2-1 – Brodifacoum loading in wild Norway rats given various feeding exposures to 50ppm Talon Pellets.

Refer Figure A7_4_2-2 – Canine secondary toxicity.

4.1.4 Other Observations

None

4.2 Estimation of bioconcentration

Not the purpose of the study.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

The test material, ground Norway rats (albino Wistar strain) administered brodifacoum, was fed to dogs to determine the secondary toxicity of brodifacoum to dogs. A guideline method was not used, but the study was conducted in accordance with accepted scientific principles of the time.

Initially, the diet preparation involved the use of Norway rats with an average body weight of 200g. Each animal was orally intubated with a solution of brodifacoum in polyethylene glycol 300. The solution was prepared containing brodifacoum at 1.5mg/ml and administered at 1mg/100g body weight. This would give each rodent a dose of 15mg of brodifacoum per kg of rat, presenting a worst-case situation and simulating feeding on 50ppm Talon Pellets until death. At death, each animal was sliced into 2 sections and ground into a 'rat meal' using a conventional electric meat grinder. Individual packs were prepared and frozen. Control rats were prepared in a similar manner. Diet was thawed for 14-16 hours before being presented to the dogs.

Seven dogs (Beagles, *Canis familiaris*) were obtained from Johnson County, North Carolina. The dogs were selected to present a realistic

model of what would be expected if a domestic dog were allowed to consume rats intoxicated with brodifacoum. Each dog was decontaminated on arrival at the laboratory.

Blood samples were taken to determine the health status of the animals.

Each animal was individually housed in runs. All animals were acclimatised for two weeks prior to the treatment, during this period they were fed canned dog food *ad lib* for 12 of the 14 days. The final two days were used to introduce and acclimatise the dogs to the 'rat meal'. For these purposes 800g of ground untreated rodents were provided to each animal.

3 groups of one male and one female were used. The groups were allocated to 1, 3 and 4 day no-choice feeding studies. One male control animal was also used. Each animal was provided with 650g of rat meal on each day for the period of the test. 650g or 75% of the usual daily consumption was used to determine complete consumption and also to reflect in nature that dogs would not be expected to have an unlimited supply of rats. Following treatment, the animals were observed for 10 days and any signs were recorded. *Post-mortem* was carried out on all animals.

5.2 Results and discussion

All consumption data was recorded and theoretical maximum doses of brodifacoum were calculated. The calculated doses do not allow for detoxification or excretion of brodifacoum or its metabolic products in the rat.

Animal 6M died after consuming 1177.1g of tissue, which was equivalent to five 200g rats. Initial blood samples suggested the dog was slightly anaemic. Animal 3M ate 1950g of tissue, the equivalent of nearly 10 200g rats and survived. Adjusted for body weight of the dogs, the doses of brodifacoum are not divergent with 2.22mg/kg for the survivor and 1.85mg/kg for the one mortality.

5.3 Conclusion

This study demonstrates that the field hazard to dogs in the form of secondary toxicity may be variable but should not be severe. Especially, when considering the high loading of the rats in the study (55 times the LD50 of brodifacoum) and the individual dog which survived a level of consumption of tissue, equivalent to nearly 10 rats.

5.3.1 Reliability 2

5.3.2 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	May 2005
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	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*
Reliability	*Discuss if deviating from view of rapporteur member state*
Findings	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

FIGURE A7_4_2-1 – BRODIFACOUM LOADING IN WILD NORWAY RATS GIVEN VARIOUS FEEDING EXPOSURES TO 50PPM TALON PELLETS.

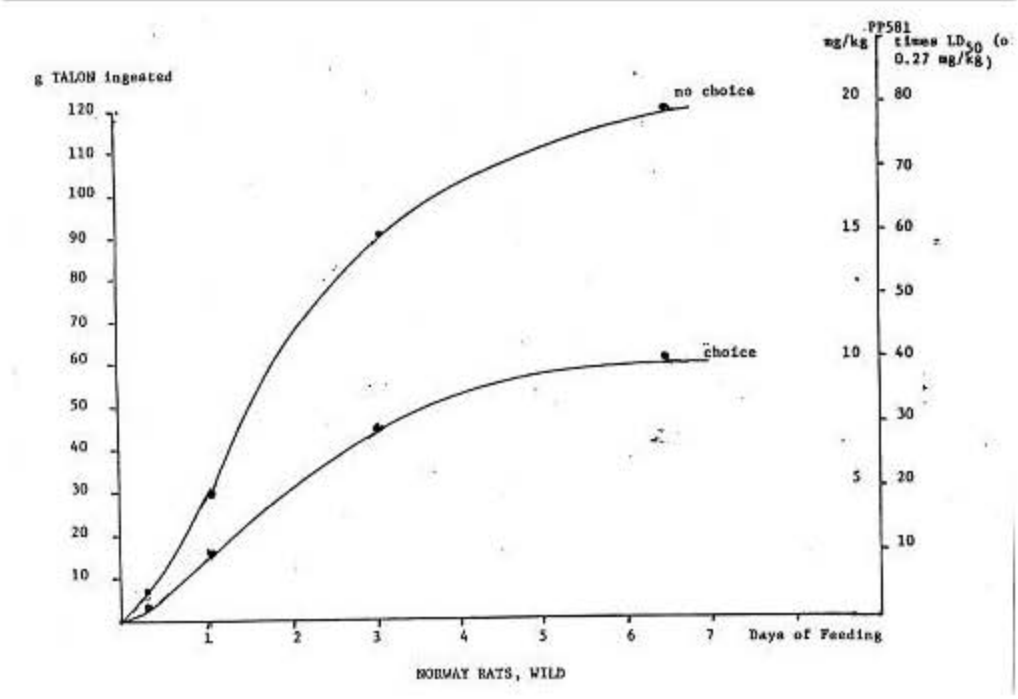
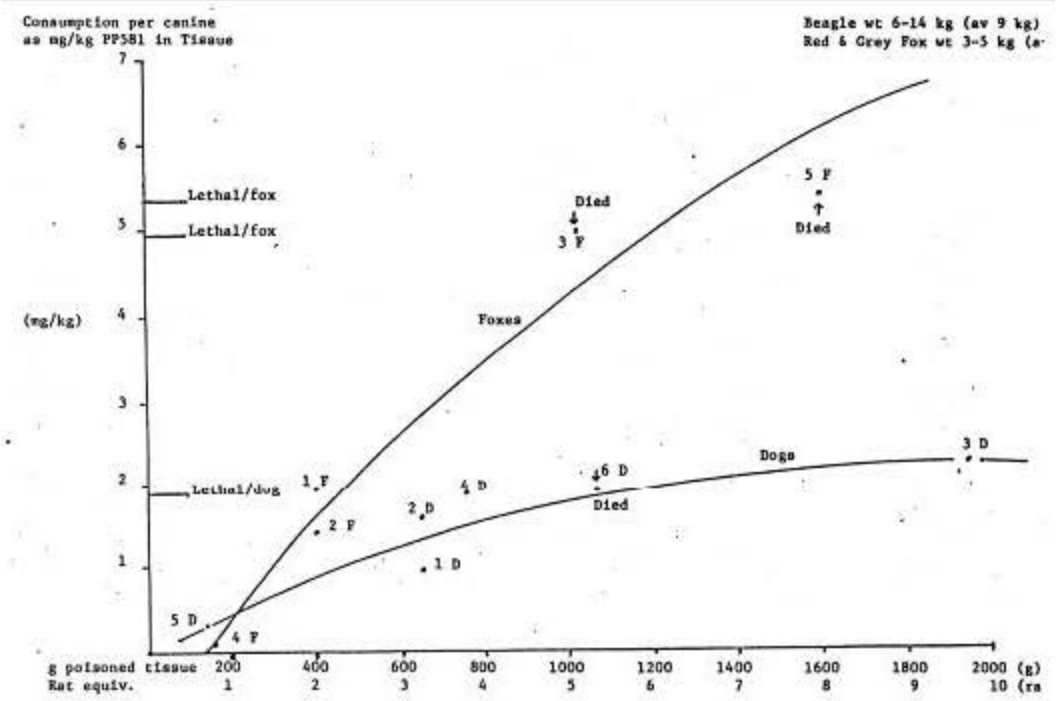


FIGURE A7_4_2-2 – CANINE SECONDARY TOXICITY.



Sorex Limited	Klerat Pellets	February 2004

Doc IIIA/Section 7.8.1(1)

BPD Data Set IIIB/Annex Point XIII.3.1

Toxicity to terrestrial vertebrates other than birds.

Secondary toxicity of brodifacoum to dogs.

Official use only

1	**REFERENCE**	
1.1	**Reference**	[redacted], 1978. Talon: Secondary toxicity of brodifacoum to dogs (Beagles), (North Carolina). ICI Americas Inc. Report Series TMUD1997/B (unpublished) [redacted].
1.2	**Data protection**	[redacted]
1.2.1	Data owner	[redacted]
1.2.2	Companies with Letter of Access	[redacted]
1.2.3	Criteria for data protection	[redacted]
2	**GUIDELINES AND QUALITY ASSURANCE**	
2.1	**Guideline study**	No guideline was stated in the report. The study was conducted in accordance with accepted scientific principles of the time.
2.2	**GLP**	No, the study pre-dates the requirements of GLP.
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	A brodifacoum solution in polyethylene glycol 300 at a dose of 1.5mg/ml (15mg of brodifacoum per kg of rat) to simulate feeding on 50ppm Talon Pellets.	
3.1.1	Lot/Batch number	Not available	X
3.1.2	Specification	Not stated	X
3.1.3	Purity	Not stated	X
3.1.4	Further relevant properties	The test material was administered to simulate rats feeding on Talon Pellets which contain a nominal concentration of 50ppm brodifacoum. The amount administered would give each rodent a dose of 15mg of brodifacoum per kg of rat, presenting a worst-case situation and simulating feeding on 50ppm Talon Pellets until death. At death, each animal was sliced into 2 sections and ground into a 'rat meal' using a conventional electric meat grinder. Individual packs were prepared and frozen. Control rats were prepared in a similar manner except that no brodifacoum was administered. Diet was thawed for 14-16 hours before being presented to the dogs.	
3.1.5	Radiolabelling	The test material was not radiolabelled.	
3.1.6	Method of analysis	None	
3.2	**Reference substance**	No	
3.2.1	Method of analysis for reference substance		
3.3	**Testing/estimation procedure**		
3.3.1	Test system/ performance	Dogs were selected to present a realistic model of what would be expected if a domestic dog were allowed to consume rats intoxicated with brodifacoum. Each dog was decontaminated on arrival at the laboratory and blood samples were taken to determine the health status of the animals. 3 groups of dogs, one male and one female, were used. The groups were allocated to 1, 3 and 4 day no-choice feeding studies. One male control animal was also used. Each animal was provided with 650g of rat meal on each day for the period of the test. 650g or 75% of the usual daily consumption was used to ensure complete consumption and also to reflect that dogs would not be expected to have an unlimited supply of rats. Following treatment, the animals were observed for 10 days and any signs were recorded. Post-mortem was carried out on all animals.	
3.3.2	Estimation of bioconcentration	Bioconcentration was not measured. The study was performed to investigate the potential for secondary toxicity to dogs if they consume rodents after the rodents have consumed a product containing the active substance, brodifacoum.	

4 RESULTS

4.1 Experimental data

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4.1.2 Food consumption

All consumption data was recorded and theoretical maximum doses of brodifacoum were calculated. These calculated theoretical doses do not allow for detoxification or excretion of brodifacoum or its metabolic products in the rat.

Amount of rats consumed, g and dose of brodifacoum ingested, mg/kg by dogs.

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4 day	6M	9.52	1177.1	1.85	9
Control	7M	8.72	0	0	-

4.1.3 Results in graphical format

Refer Figure A7_4_2-1 – Brodifacoum loading in wild Norway rats given various feeding exposures to 50ppm Talon Pellets.

Refer Figure A7_4_2-2 – Canine secondary toxicity.

4.1.4 Other Observations

None

4.2 Estimation of bioconcentration

Not the purpose of the study.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

The test material, ground Norway rats (albino Wistar strain) administered brodifacoum, was fed to dogs to determine the secondary toxicity of brodifacoum to dogs. A guideline method was not used, but the study was conducted in accordance with accepted scientific principles of the time.

Initially, the diet preparation involved the use of Norway rats with an average body weight of 200g. Each animal was orally intubated with a solution of brodifacoum in polyethylene glycol 300. The solution was prepared containing brodifacoum at 1.5mg/ml and administered at 1mg/100g body weight. This would give each rodent a dose of 15mg of brodifacoum per kg of rat, presenting a worst-case situation and simulating feeding on 50ppm Talon Pellets until death. At death, each animal was sliced into 2 sections and ground into a 'rat meal' using a conventional electric meat grinder. Individual packs were prepared and frozen. Control rats were prepared in a similar manner. Diet was thawed for 14-16 hours before being presented to the dogs. X

Seven dogs (Beagles, *Canis familiaris*) were obtained from Johnson County, North Carolina. The dogs were selected to present a realistic

		model of what would be expected if a domestic dog were allowed to consume rats intoxicated with brodifacoum. Each dog was decontaminated on arrival at the laboratory. Blood samples were taken to determine the health status of the animals. Each animal was individually housed in runs. All animals were acclimatised for two weeks prior to the treatment, during this period they were fed canned dog food *ad lib* for 12 of the 14 days. The final two days were used to introduce and acclimatise the dogs to the 'rat meal'. For these purposes 800g of ground untreated rodents were provided to each animal. 3 groups of one male and one female were used. The groups were allocated to 1, 3 and 4 day no-choice feeding studies. One male control animal was also used. Each animal was provided with 650g of rat meal on each day for the period of the test. 650g or 75% of the usual daily consumption was used to determine complete consumption and also to reflect in nature that dogs would not be expected to have an unlimited supply of rats. Following treatment, the animals were observed for 10 days and any signs were recorded. *Post-mortem* was carried out on all animals.	
5.2	**Results and discussion**	All consumption data was recorded and theoretical maximum doses of brodifacoum were calculated. The calculated doses do not allow for detoxification or excretion of brodifacoum or its metabolic products in the rat. Animal 6M died after consuming 1177.1g of tissue, which was equivalent to five 200g rats. Initial blood samples suggested the dog was slightly anaemic. Animal 3M ate 1950g of tissue, the equivalent of nearly 10 200g rats and survived. Adjusted for body weight of the dogs, the doses of brodifacoum are not divergent with 2.22mg/kg for the survivor and 1.85mg/kg for the one mortality.	X
5.3	**Conclusion**	This study demonstrates that the field hazard to dogs in the form of secondary toxicity may be variable but should not be severe. Especially, when considering the high loading of the rats in the study (55 times the LD50 of brodifacoum) and the individual dog which survived a level of consumption of tissue, equivalent to nearly 10 rats.	
5.3.1	Reliability	2	
5.3.2	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	May 2005
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
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*
Reliability	*Discuss if deviating from view of rapporteur member state*
Findings	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

FIGURE A7_4_2-1 – BRODIFACOUM LOADING IN WILD NORWAY RATS GIVEN VARIOUS

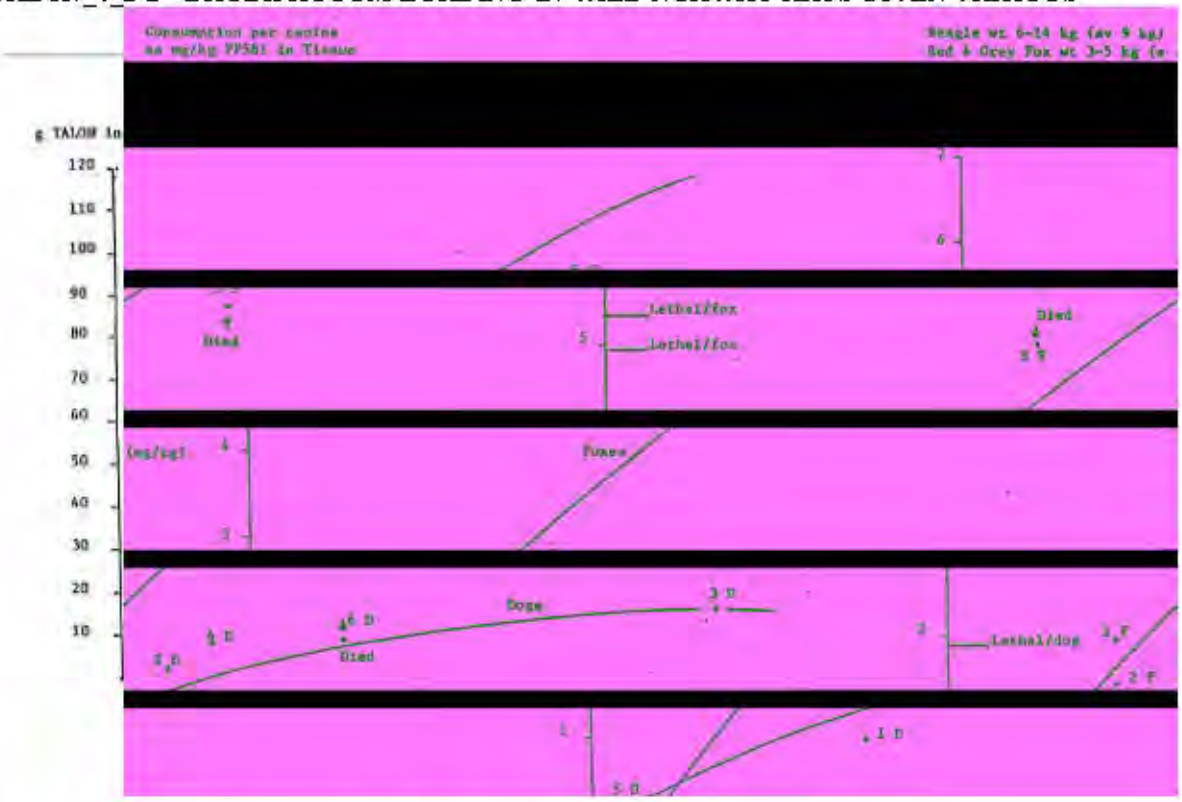
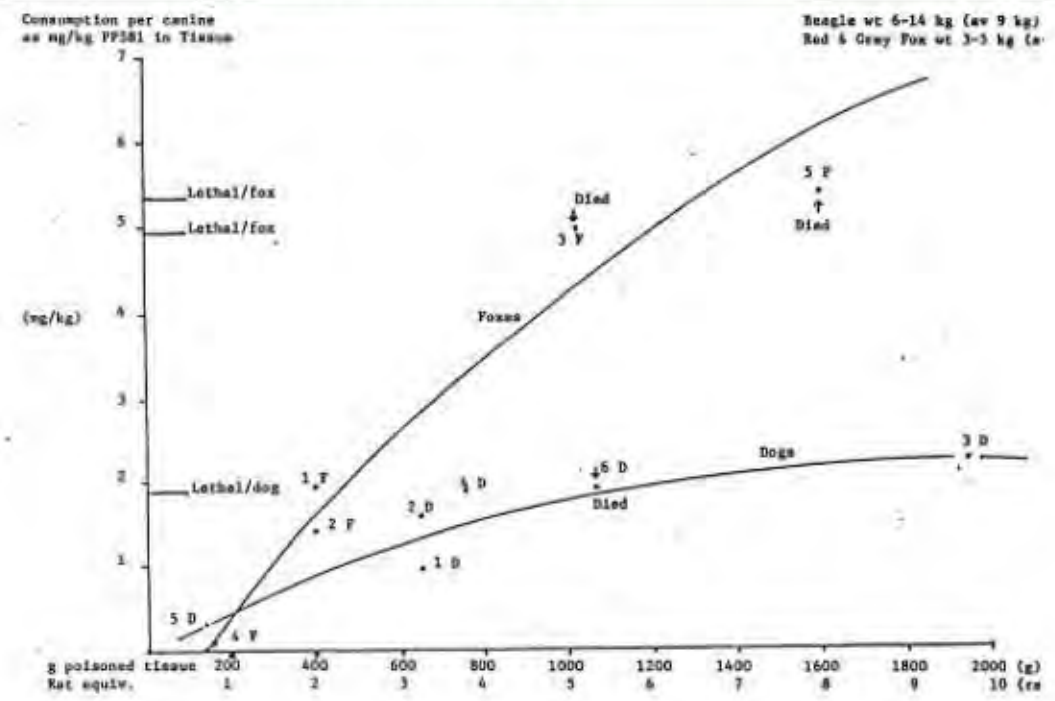


FIGURE A7_4_2-2 – CANINE SECONDARY TOXICITY.



Doc IIIA / Section 8

BPD Data Set IIA / Annex Point VIII.8

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 (Annex IIA, point 8.1)

Handling and Use

Avoid contact with skin and eyes. Do not breathe dust.

Storage

Keep container tightly closed, in a cool, well-ventilated place. Keep away from moisture. Stable as a solid at 50 Deg C.

Transport

UN No 3027, UN Proper Shipping Name COUMARIN DERIVATIVE PESTICIDE, SOLID, TOXIC.

Fire

Keep fire exposed containers cool by spraying with water. For small fires, use foam, carbon dioxide or dry powder extinguishant. For large fires, use foam or water-fog; avoid use of water jet. Contain run-off water with, for example, temporary earth barriers. A self contained breathing apparatus and suitable protective clothing should be worn in fire conditions.

8.2 In case of fire, nature of reaction products, combustion gases, etc. (Annex IIA, point 8.2)

Combustion or thermal decomposition will evolve toxic and irritant vapours.

Doc IIIA / Section 8

Measures necessary to protect man, animals and the environment

BPD Data Set IIA / Annex Point VIII.8

8.3 Emergency measures in case of an accident (Annex IIA, point 8.3)

First Aid

Eyes: Immediately irrigate with eyewash solution or clean water holding the eyelids apart, for at least 15 minutes. Obtain immediate medical attention.

Skin: Take off immediately all contaminated clothing. Wash skin immediately with water, followed by soap and water. Such action is essential to minimise contact with skin. Contaminated clothing should be laundered before re-issue.

Ingestion: TRANSFER TO HOSPITAL IMMEDIATELY.
Refer to the leaflet 'The treatment of Anticoagulant Rodenticide Poisoning', 1988. Induce vomiting, if this has not already occurred by tickling the back of the throat with a clean, blunt instrument (e.g. spoon handle).

Inhalation: Unlikely to be hazardous by inhalation unless present as a dust. Remove patient from exposure, keep warm and at rest. Obtain medical attention as a precaution. Remove from exposure. Obtain medical advice immediately.

Advice to physicians: Gastric lavage may be effective when performed within 4 hours of ingestion. Doctors should refer to the leaflet 'The treatment of Anticoagulant Rodenticide Poisoning', 1988.

Environmental

Spillages or uncontrolled discharges into water courses must be alerted to the appropriate regulatory body. Cover spillage with moist sand, soil or sawdust. Transfer to a container for disposal. Wash the spillage area with water. Washings must be prevented from entering surface water drains.

8.4 Possibility of destruction or decontamination following release in or on the following: (a) air (b) water, including drinking water (c) soil (Annex IIA, point 8.4)

Any contaminated materials must be disposed of as controlled waste. Disposal should be in accordance with local, state or national legislation.

8.5 Procedures for waste management of the active substance for industry or professional users

8.5.1 Possibility of re-use or recycling (Annex IIA, point 8.5.1)

Re-use and recycling are not recommended.

The product should only be used for the intended purpose: A coumarin- type anticoagulant rodenticide.

8.5.2 Possibility of neutralisation of effects (Annex IIA, point 8.5.2)

Incineration is the recommended method of disposal.

Doc IIIA / Section 8 — **Measures necessary to protect man, animals and the environment**

BPD Data Set IIA / Annex Point VIII.8

8.5.3	**Conditions for controlled discharge including leachate qualities on disposal (Annex IIA, point 8.5.3)**	Not applicable. Discharge is not permitted.
8.5.4	**Conditions for controlled incineration (Annex IIA, point 8.5.4)**	Any disposal should be in accordance with local, state or national legislation.
8.6	**Observations on undesirable or unintended side-effects, e.g. on beneficial and other non-target organisms (Annex IIA, point 8.6)**	Refer to Chapter 5 above and DocIIIA5.

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*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*
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	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	
	COMMENTS FROM ...
Date	
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Reliability indicator	1