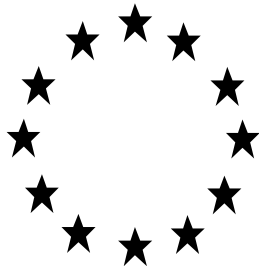
Directive 98/8/EC concerning the placing of biocidal products on the market

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

Assessment Report



Chlorophacinone

Product-type 14 (Rodenticides)

20 February 2009

Annex I - Spain

Chlorophacinone (PT 14)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 20 February 2009 in view of its inclusion in Annex I to Directive 98/8/EC

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

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

Chlorophacinone (CAS no. 3691-35-8) was notified as an existing active substance, by LiphaTech S.A.S, hereafter referred to as the applicant, in product-type 14.

Commission Regulation (EC) No 1451/2007 of 4 December 2007[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 7(1) of that Regulation, Spain was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for chlorophacinone as an active substance in Product Type 14 was 28 March 2004 in accordance with Article 9(2) of Regulation (EC) No 1451/2007.

On 27 March 2004, the Spanish competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 28 September 2004.

On 31 January 2006, the Rapporteur Member State submitted, in accordance with the provisions of Article 14(4) and (6) of Regulation (EC) No 1451/2007, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 21 February 2006. The competent authority report included a recommendation for the inclusion of Chlorophacinone in Annex I to the Directive for product-type 14.

In accordance with Article 16 of Regulation (EC) No 1451/2007, the Commission made the competent authority report publicly available by electronic means on 15 June 2006. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

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

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 1451/2007 of 4 December 2007 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. OJ L 325, 11.12.2007, p. 3

On the basis of the final competent authority report, the Commission proposed the inclusion of Chlorophacinone in Annex I to Directive 98/8/EC and consulted the Standing Committee on Biocidal Product on 20 February 2009.

In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 20 February 2009.

1.2. Purpose of the assessment report

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

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

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

1.3. Overall conclusion in the context of Directive 98/8/EC

The overall conclusion from the evaluation is that it may be expected that there are products containing chlorophacinone 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, as it poses in particular unacceptable environmental risk to non-target animals. However, chlorophacinone is for the time being considered essential for reasons of public health and hygiene, which justifies its inclusion 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

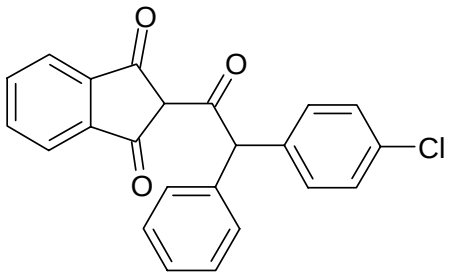
3 http://ec.europa.eu/comm/environment/biocides/index.htm

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.	3691-35-8
EINECS-No.	223-003-0
Other No. (CIPAC, ELINCS)	CIPAC No. 208
IUPAC Name	2-[2-(4-chlorophenyl)-2-phenylacetyl]indan-1,3-dione *
Common name, synonym	Chlorophacinone
Molecular formula	$C_{23}H_{15}ClO_3$
Structural formula	
Molecular weight (g/mol)	374.82
Purity: % w/w (specification):	>97.8%
Isomeric composition	Chlorophacinone contains one optically active carbon and therefore exists as two enantiomers. The ratio of the enantiomers is provided in the confidential file
Impurities and additives:	Information on the impurities and additives in the technical grade active substance is confidential to LiphaTech S.A.S. and is presented in the confidential attachment.

* This is the correct IUPAC name for chlorophacinone. Until 2007 the IUPAC name for this compound was considered to be 2-[(4-chlorophenyl)phenylacetyl]-1H-indane-1,3-(2H)-dione

Chlorophacinone is a pale yellow odourless powder at room temperature. Its density, 1.4301 g/mL is greater than water although its bulk density is 0.35 g/mL. It does not undergo thermal decomposition below it melting temperature, which is in the region of 141°C, but it starts to decompose at 250 ºC without boiling. Although its solubility in purified water is very low (13 mg/L at 20°C) making the determination of pKa difficult, solubility in buffered water is pH dependent (pH 4: 1 mg/L at 20ºC; pH 7: 344 mg/L at 20ºC; pH 10: 476 mg/L at 20ºC). Its vapour pressure is low (4.76×10^{-4} Pa at 23ºC) and hence its Henry's Law Constant (0.013725 $Pa.m^3.mol^{-1}$) indicates that volatilisation is not expected to significantly contribute to the dissipation of chlorophacinone in the environment. Chlorophacinone is not surface active and its octanol:water partition coefficient is also pH dependant although the value of Log P_{ow} at neutral pH is below 3 indicating that it is unlikely to bioaccumulate (Log P_{ow} = 3.08 (pH 4), Log P_{ow} = 2.42 (pH 7), and Log P_{ow} = 2.57 (pH 9)). Chlorophacinone is poorly (<1%) soluble in methanol and hexane.

Adequate methodology exists for the determination of the active substance in the technical active substance, in the individual products and in soil, water, air blood and liver tissues. Analytical methods have been developed to determine residues of chlorophacinone in food and feeding stuff.

2.1.2. Intended Uses and Efficacy

2.1.2.1. Field of use envisaged / Function and organism(s) to be controlled

Chlorophacinone is used as a rodenticide pest control substance (Main group 03, product type 14), to control *Rattus norvegicus* (Norway rat, Brown rat) and *Mus musculus* (House mouse).
In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, and to apply adequately the provisions of Article 5(1) of Directive 98/8/EC and the common principles laid down in Annex VI of that Directive, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.2.2. Effects on target organisms

Chlorophacinone is a first-generation anticoagulant rodenticide. It disrupts the normal blood clotting mechanisms resulting in increased bleeding tendency and, eventually, profuse haemorrhage and death and interfering the vitamin K in the 'clotting cascade' that involves numerous clotting factors. Effectiveness of the active substance depends on exposure (i.e. consumption of the bait by the target organism). Generally, effects can be observed using bait concentrations of 5 mg/kg or more. However, for effective and comprehensive control of rats and mice, a bait concentration of 50 mg/kg is proposed. The formulated product type has no significant difference on the effects of the active substance on the target organisms.

2.1.2.3. Humaneness

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

2.1.2.4. Efficacy studies with Product P1

A laboratory efficacy study has been conducted with rats using block bait containing 50 mg/kg chlorophacinone. Two free-choice laboratory tests were conducted with rats (wild-strain warfarin-sensitive *Rattus norvegicus*). Exposure to the treated bait for 4 days produced 100% and 90% efficacy (mortality) for the respective tests, death occurring between 7 and 17 days. Consumption of the bait was considered good.

Consumption of the treated block bait was good in the laboratory test and was sufficient to produce high mortality rates.

In conclusion, Product P1 blocks are sufficiently attractive and produce sufficient mortality to classify the efficacy of the product as excellent.

2.1.2.5. Efficacy studies with Product P2

Chlorophacinone is a well established rodenticide which has been in effective use for over 20 years formulated in a number of products including blocks and grains.

A number of laboratory efficacy studies have been conducted with mice and rats using grain baits containing 50 mg/kg chlorophacinone. Four free-choice laboratory tests were conducted with rats (wild-strain coumafene-sensitive *Rattus norvegicus*). Exposure to the treated bait was for four days and five days. Efficacy (mortality) was 100% for the five day exposure and 90% for the four day exposure tests, with deaths occurring from 4 to 17 days after start of treatment.

A free-choice laboratory tests were conducted with mice (wild-strain warfarin-sensitive *Mus musculus*). Exposure to the treated bait was for four days giving a 96% efficacy (mortality) with deaths occurring between 5 and 11 days.

Palatability of the treated pellets was generally good in the laboratory tests (Attractivity between 0.38 and 0.57) and the consumption was sufficient to produce high mortality rates.

In conclusion, Product P2 is sufficiently attractive and produces sufficient mortality to classify the efficacy of the product as excellent.

2.1.2.6. Efficacy studies with Product P3

A number of laboratory studies have been conducted with mice and rats using tracking powder containing 2000 mg/kg chlorophacinone. Four laboratory tests were conducted where rats (laboratory bred, wild-strain coumafene-sensitive *Rattus norvegicus*) were allowed to walk through treated tracking powder. Exposure to the tracking powder was for one or four days. The efficacy (mortality) was 100% for both exposure times. Mortality was observed from 7 to 16 days following first exposure to the powder.

Two laboratory tests were conducted where mice (laboratory bred, wild-strain warfarin-sensitive *Mus musculus*) were allowed to walk through treated tracking powder. Exposure to the tracking powder was for one or four days. The efficacy (mortality) was 93% for the four days exposure and 100% for the one day exposure. Mortality was observed from 4 to 21 days following first exposure to the powder.

Ingestion of the product via grooming was sufficient to produce high mortality rates in the laboratory studies.

In conclusion, Product P3 produces sufficient mortality to classify the efficacy of the product as excellent.

2.1.3. Classification and Labelling

2.1.3.1. Proposal for the classification and labelling of the active substance

Hazard symbol:	T+,N	
Risk phrases	R26/27/28 R48/23/24/25 R61 R50/53	Very toxic by inhalation in contact with skin and if swallowed. Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed. May cause harm to the unborn child Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety phrases	S(1/2) S36/37 S45 S53 S60 S61	Keep locked up and out of reach of children. Wear suitable protective clothing and gloves In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible). Avoid exposure - obtain special instructions before use This material and its container must be disposed of as hazardous waste Avoid release to the environment. Refer to special instructions/safety data sheets.
Specific concentration limits	C≥0.7% 0.5%≤C<0.7% 0.1%≤C<0.5% 0.07%≤C<0.1% 0.01%≤C<0.07% 0.001%≤C<0.01%	T^+; R61- 26/27/28- 48/23/24/25 T^+; R61-26/27-25-48/23/24/25 T^+; R26/27-25-48/23/24/25 T^+; R26/27-22-48/20/21/22 T; R23/24-22-48/20/21/22 Xn; R20/21

Justification for the proposal

Chlorophacinone is thermally stable up to 143°C, its melting point. It is not classified as highly flammable and does not undergo self ignition below its melting point. It is not explosive nor does it have oxidising properties. There is no record that it has reacted with any storage container during many years of industrial production. Therefore, there are no physical chemical related hazards associated with normal use of the active substance.

The safety phrases proposed are based on the classification and risk phrases. On basis of study results from studies presented in the dossier classification of chlorophacinone was proposed according to principles detailed in Annex VI of Council Directive 67/548/EEC (with amendments and adaptations).

The classification for human health effects of chlorophacinone is in May 2007 still under discussion. For anticoagulant rodenticides, regarding human health effects, a provisional classification with R61 was decided in November 2006 by the C & L, but without a final decision on the category to be used (Repr. Cat.1 or Repr. Cat. 2). The proposed classification for chlorophacinone for acute and repeated dose toxicity was agreed in May 2007. At that moment, the provisionally classification for reprotoxicity was not confirmed as the TC C& L decided to await further results from studies on anticoagulant rodenticides before finalising the discussion on reprotoxicity. Specific concentration limits for chlorophacinone are proposed, but there are still under consideration.

The acute toxicity of chlorophacinone in fish, daphnia and algae was investigated, so that sufficient data are available to allow classification and labelling of the active ingredient according to the requirements of Annex VI of directive 67/548/EEC. The proposed classification and labelling (R50) is based upon acute toxicity testing in aquatic organism (fish LC_{50} (96 h) = 0.45 mg a.s/l, EC_{50} (48 h) = 0.64 mg a.s/l, algae $E_r C_{50}$ (72 h) = 2.2 mg a.s/l). Chlorophacinone was also tested for ready biodegradability under aerobic conditions at a mean temperature of 22°C in the dark over a period of 28 days (inoculum used: aerobic activated sewage sludge from a treatment plant). It was concluded not being readily biodegradable. An investigation into the inherent biodegradability was not carried out since the notifier assumed that chlorophacinone is not inherently biodegradable. It has also been assumed by the notifier that chlorophacinone is not likely to be biodegradable in biological sewage treatments either under aerobic or under anaerobic conditions. The conclusion was that chlorophacinone is not biodegradable under environmentally relevant conditions or expected to be biodegradable during sewage treatment processes (R 53).

2.1.3.2. Proposal for the classification and labelling of of products P1 and P2

PRODUCT P1	
Classification	**as detailed in Directive 67/548/EEC**
Class of danger	
R phrases	
S phrases	**S2:** Keep out of the reach of children. **S13:** Keep away from food, drink and animal feedingstuffs. **S24:** Avoid contact with skin. **S35:** This material and its container must be disposed of in a safe way. **S46**: If swallowed, seek medical advice immediately and show this container or label.

PRODUCT P2	
Classification	**as detailed in Directive 67/548/EEC**
Class of danger	
R phrases	
S phrases	**S2:** Keep out of the reach of children. **S13:** Keep away from food, drink and animal feedingstuffs. **S22:** Do not breathe dust. **S35:** This material and its container must be disposed of in a safe way. **S36/37:** Wear suitable protective clothing and gloves. **S45**: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

Justification for the proposal

Specific concentration limits for human health are still under discussion. If the proposed specific concentration limits are accepted, the chlorophacinone containing products (blocks and grains) will be classified because the concentration of the active substance in the products is equal to the proposed specific concentration limits for the classification of the products with R20/21. However, no classification for dermal toxicity is needed as the study results on the products do not meet the classification criteria. No acute inhalation studies on the products are

presented, but the physical nature of these products is such that classification for acute inhalational toxicity is not considered needed.

2.1.3.3. Proposal for the classification and labelling of products P3

PRODUCT P3	
Classification	**as detailed in Directive 67/548/EEC**
Class of danger	**T; Xn**
R phrases	**R25:** Toxic if swallowed **R20/21:** Harmful by inhalation and in contact with skin.
S phrases	**S2:** Keep out of the reach of children. **S13:** Keep away from food, drink and animal feedingstuffs. **S22:** Do not breathe dust. **S35:** This material and its container must be disposed of in a safe way. **S36/37:** Wear suitable protective clothing and gloves. **S45**: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

Justification for the proposal

On basis of study results presented in the dossier, it is proposed to change the current classification of Product P3 from R20/21/22 to R20/21 and R25.

Specific concentration limits for human health are still under discussion. If the proposed specific concentration limits are accepted, the product P3 containing 0.2% chlorophacinone will be classified as T+; R26/27-25-48/23/24/25 because the concentration of the active substance in the products is in the range of 0.1%≤C<0.5%.

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification and effect assessment

Metabolism

Chlorophacinone is absorbed following oral administration. The compound is absorbed, enters the enterohepatic circulation and then is excreted through the faeces. Metabolism studies in rats with radiolabelled Chlorophacinone showed that it is absorbed following oral administration, with a relatively short (10.2 hours) plasma half-life. After a single low dose (1-1.4 mg/Kg), 100% of the administered material is excreted within 4 days. Higher doses (2 mg/kg) showed that at 168 hours excretion is incomplete and 8% of dose was still present in the carcass. Elimination was mainly via faeces, with less than 1% of urinary excretion, and no excretion via expired air.

About 19.6% of the faecal radioactivity (equivalent to 15% of dosed radioactivity) is unchanged parent compound and most were metabolised compounds. Two main metabolites were identified as hydroxylated metabolites accounting for the 45% of faecal radioactivity

(36.2% of administered dose) with some “minor” unidentified metabolites representing 34% of faecal radioactivity. It is important to note that a peak representing 12.49 % of assigned peaks (representing about 8 % of dosed radioactivity) was detected but not identified.

The applicant argued that "none of the metabolites identified have been shown to be toxicologically significant". However no data is presented to justify this statement.

Dermal absorption

In an *in vitro* test of dermal penetration with human skin, Chlorophacinone showed rapid absorption but with minimal total absorption. The highest proportion detected in the receptor fluid was 0.44 % which represents the actual systemic proportion. Total absorption was estimated to be 1.7% for the human including radioactivity measured in receptor fluid, tape stripping and residual skin values.

Acute toxicity

The best conducted oral acute toxicity test is that in rat (A 6.1-01), showing lethality at all doses, gave as a result a critical value of LD50 of 3.15 mg/kg bw (males). Based on this value, a classification with R 28 ‘*Very toxic if swallowed’* is deduced. In a study in dogs (fed with vitamin K deficient diet), all males died at all doses including the lowest tested dose (2 mg/kg bw).

Dermal acute exposure of Chlorophacinone elicited limited lethality at all dose levels enabling a determination of the dermal LD50 of 0.329 mg/kg in the acute toxicity study in rabbits. Consequently, Chlorophacinone is classified with R27 ‘*Very toxic in contact with the skin’*.

The acute inhalation LC50 for technical Chlorophacinone when administered undiluted as a dust to albino rats was calculated to be 7.00 µg/L (0.83-59.0 µg/L) for males, 12.00 µg/L (7.80-18.0) for females, and 9.30 µg/L (2.30-38.0) for males-females, lower than the limit in the criteria for classification as R26 (0,25 mg/litre/4h). Therefore, the acute toxicity study is not supporting the current classification as R23 and it should be classified as R26.

Inhalation toxicity by long term exposure can also be applied considering the relationship with the criteria for R48. No data are available for repeated inhalation toxicity but the application of R48 may be extrapolated for applying also with R23 as R48/23/24/25.

The studies on skin/eye irritancy and sensitisation were negative, leading to no classification.

In short: Chlorophacinone requires labelling with the symbol T+ and the risk phrases R26/27/28 *Very toxic by inhalation in contact with skin and if swallowed and* R48/23/24/25 *Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.* Chlorophacinone is not classified as a skin irritant, eye irritant or skin sensitiser.

Repeated toxicity

The toxicity response of Chlorophacinone shows very “drastic” dose-effect relationship (high slope in dose-response curve). The toxic doses are lethal showing lethality after some time of repeated dosing. In most studies, the next dose higher than NOAEL is showing high lethality due to haemorrhage, although in some case it is possible to observe a dose with low lethality

with altered coagulant parameter (as prothrombin time). The anticoagulant property of Chlorophacinone is responsible of the toxicity and no other effects are significant in comparison with the so relevant anticoagulant property. At higher doses, lethality occurs at shorter time whereas at lower doses lethality only occurs after longer time of repeated dosing but in any case after an accumulative time of repetitive dosing, haemorrhage is causing lethality.

Repeated dermal toxicity (21 days study)

There are not specific acceptable data available for repeated dose dermal exposure with the active substance. There is a range finding study which is useful to confirm the value of the available study with the formulation tracking power. A full study was performed with the formulation tracking power containing 0.2 % of active substance in New Zealand White rabbits. The study allows obtaining NOAEL by dermal exposure as 0.08 mg/kg/d in rabbit dosed as tracking power formulation being the most sensitive observation the alteration of prothrombin times which was observed at 0.4 and 2 mg/kg/day. No data of dermal absorption are available in rabbit skin, so the dermal repeated study in rabbit cannot be directly used for estimating the no-effect systemic dose, and consequently no direct use can be done for risk characterization by comparison with systemic dose estimated for human exposure.

Subchronic oral toxicity in rats

A study intended for evaluating the subchronic oral toxicity for a period exceeding 90 days, were performed dosing Chlorophacinone, dissolved in corn oil, administered by gavage (oral intubation) to rats, 7 days/week at dosages of 0, 5, 10, 20, 40, 80, 160 µg/kg bw per day for a period ranging from 11 to 16 weeks. The study was conducted according to EC Method B.27 guidelines with some deficiencies: limited microscopic examination, clinical signs were not reported for each dose group. The low dose group was terminated after 11 weeks (77 days) (justified by Authors as due to the complete absence of any toxicological effects at this dose). An uncertainty for a definitive adoption of NOAEL/LOAEL is that coagulation activity was not monitored at the lowest dose of 5 µg/kg bw/day, just the dose that later is proposed for NOAEL. It is technically and operationally justified but in any case some uncertainty is maintained. The study is accepted but with the commented uncertainty.

No mortality was noted at 5 µg/kg over the 11 weeks of study. One male and one female of 10 µg/kg died but was interpreted as due to intubation error and not considered for evaluation. Mortality was noted in all dosage groups above 10 µg/kg. High mortality is observed at dose 20 µg/kg/d of higher for males and 40 µg/kg/d or higher for females. The dominant clinical signs were related to the anticoagulant activity of Chlorophacinone and were responsible for death of animals. Alteration in coagulation parameters (Quick test time) were notably pronounced in groups 20 and 40 µg/kg and were minimal in group 10 µg/kg/day but significantly different from controls. A LOAEL of 10µg/kg/day is established on the basis of 16 weeks dosing period with minimal increase but statistically significant in coagulation time and other biochemical parameters alteration which are suggestive of hepatic and renal disorders. It is concluded that for subchronic oral toxicity NOAEL value of 5 µg/kg bw/day can be established based on results from 11 weeks (77 days) administration. An uncertainty is maintained on this conclusion as no coagulation time was measured at this dose and this group was terminated before the 90 days. The uncertainty in NOAEL/LOAEL is considered for risk characterization.

A repeat dose inhalation study is not presented. Applicant argue that considering the acute inhalation toxicity and the anticoagulant properties, an inhalation repeated dose study as it will result in death by induction of a haemorrhagic syndrome including at low dose. Therefore if these arguments for waiving of repeated inhalation study is accepted, it involves accepting that is actually "very toxic by inhalation" and R26 should be applied.

Chlorophacinone was not mutagenic in a standard range of *in vitro* and *in vivo* tests. Chlorophacinone shows two metabolites: both are hydroxylated forms of the parent material. The structural similarity to the parent material (active substance) is such that further mutagenicity studies on the metabolites are considered unnecessary.

Carcinogenicity and long-term toxicity studies are not submitted and Applicant present a justification on the basis of the knowledge of mechanism of toxicity and technical difficulties to test so low dose needed for a long term exposure without lethality, taking into account the knowledge of another anticoagulant substance (warfarin, used as a human pharmaceutical for several decades) acting by the same mechanism. The 90 day study in rats showed no indications of either hyperplasia or hypertrophy at near-term lethal levels of administration.

Chlorophacinone was not embryotoxic or teratogenic in guideline studies in rat and rabbit. A 2-generation study in the rat is not presented.

It is a matter of discussion if the standard teratogenicity test is appropriate for anticoagulant rodenticides. Classification of all anticoagulant rodenticides from read across from warfarin has been suggested on the basic of the embryotoxicity properties of warfarin.

As with carcinogenicity, the primary reason for not requiring such a study is the long-term use of the structurally similar molecule warfarin in humans. There have been no indications of any adverse effects on human fertility (i.e. mating performance) of either sex undergoing treatment with anticoagulants. Therefore a study in rats would not add to the sum of knowledge on the subject.

The absence of sedative activity, anticonvulsant activity, antidepressant activity and the absence of any clinical signs in rodent and dog toxicity tests with Chlorophacinone also support the conclusion that Chlorophacinone shows no neurotoxic effects.

Human cases of acute intoxications

The applicant indicates that there are no published data on specific cases of Chlorophacinone intoxication in humans. Probably this is true for long term exposure, and no case reports from the manufacturer concerning adverse effects in users applying the products. However the WHO monographs on rodenticides (EHC; 175 showed 3 published data on persons intoxicated by suicide purpose with Chlorophacinone at doses of 625 mg, 100 mg and unknown in a third one. In all of the three cases, alterations in prothrombin time and prothrombin level were affected and intensive therapy with Vitamin K of analogues were required and no death occurred. Human data cannot be used to derive a NOAEL either for short or long term exposure.

Data and safety factors used for deducing AOEL

AOEL for repeated exposure scenarios (subchronic and chronic)

The derivation of an Acceptable Operator Exposure Level (AOEL) value for repeated use is based on the NOAEL established in a 90-day study in the rat (no dog study was performed). The NOAEL established in the rat study was 5 µg/kg/day. Nevertheless, the 5 µg/kg/day group

was terminated at week 11 and coagulation (quick) time was not determined. Hence, there is some uncertainty about whether 5 µg/kg bw/day can be considered as NOEL on the basis of coagulation quick time (significant increases of the coagulation quick time were noted in 10-µg/kgbw/day males). Therefore, an application of an additional assessment factor may be considered appropriate. Furthermore, it is not sure that rat is the most sensitive species as in a dog (fed with vitamin K deficient diet) dogs were more sensitive than rats. An additional factor of 3 has been proposed for all anticoagulant rodenticides. This could cover the above mentioned uncertainty. The standard factors of 10 for both inter and intraspecies were considered adequate.

Therefore, based on the NOEL value of 0.005 mg/kg/day derived from the 11-week rat study and a total assessment factor of 300, an AOEL of 0.000017 mg/kg bw/day was calculated.

NOAEL and AOEL for single use (acute exposure)

None of the rat (oral and inhalation exposure), rabbit (dermal exposure) and dog (oral exposure) acute studies investigated sublethal or clinical effects, i.e. prothrombin time. Thus, they are not appropriate for risk characterisation.

The acute AOEL for risk characterization was deduced from the lowest relevant NOAEL for maternal toxicity in teratogenicity studies. A value of NOAEL of 10 µg/kg bw/day on the basis of mortality in rabbit was adopted. Clinical signs of toxicity and necropsy pathology demonstrated that mortality in rats and rabbits was due to internal haemorrhage caused by the anticoagulant properties of the substance. Treatment-related clinical observations were limited to doses causing mortality prior to death. There were no treatment-related clinical signs of toxicity at lower doses. At scheduled necropsy, there were no treatment-related findings in surviving pregnant animals.

Due to the severity of the effects an extra assessment factor of 3 may be applied with a total assessment factor of 300.

Therefore, based on the NOEL value of 0.010 mg/kg/day derived from systemic toxicity in teratogenicity study in rabbits and a total assessment factor of 300, an AOEL of 0.000033 mg/kg bw/day was calculated.

2.2.1.2. Exposure assessment and risk characterisation

The products Product P1 (a cereal grain wax block) and Product P2 (a cereal grain bait) are ready to use formulations containing chlorophacinone at 50 ppm. In standard acute toxicity tests, neither formulation met the criteria for classification: they are not classed as harmful if swallowed or harmful in contact with skin; their physical nature is such that they are not capable of inhalation exposure. They are not irritant to skin or eyes, and they are not sensitisers.

The product P3 (a talc-based tracking powder) is a ready to use formulation containing chlorophacinone at 0.2%. In standard acute toxicity tests, it was classified as toxic by the oral, and harmful by dermal and inhalation routes. It was not an irritant to skin or eyes, and was not a sensitiser. The product requires labelling with the hazard symbol T Toxic and the Risk phrases R 20 Harmful by inhalation, R 21 Harmful in contact with the skin and R25 Toxic if swallowed.

Human health risk for professional users

High margins of safety exist for professional operators applying both Product P1 and Product P2 on a daily basis. Considering that gloves are (are not) worn, the margins of exposure for Product P1 / Product P2 uses were much higher than 300 (the adopted assessment factor) in all cases when gloves are worn, and around 250 when gloves are not worn with product P1 (see Table *Summary of risk assessment for professional operators)*. Based on more realistic measured values taken from an operator exposure study, the margins of safety were significantly higher than those based on default values. Regarding the use of both Product P1 and Product P2 on a single occasion, the margins of safety are supposedly higher than those of the use of Product P2 on a daily basis.

With respect to professional operators applying Product P3 on a daily basis, the margins of safety considering that gloves are worn were higher than 300 (the adopted assessment factor). If as a worst case it is considered that gloves are not used, the margins of exposure were as low as 70 based on default values in the HSL model. It has to be highlighted that some uncertainties emerge from models (BBA model: Mixing and loading model 5, page 137 TNsG Human Exposure, June 2002); and HSL model: Consumer product spraying and dusting model 2, page 199, TNsG Human Exposure, June 2002) used in the estimation of the exposure. Nevertheless, as they are overestimating the real exposure and the derived risk with gloves is acceptable, it can be concluded that these models can be used.

It is concluded that professional users handling all products containing chlorophacinone do not result in an unacceptable health risk. A summary of the risk assessment for professional operators is presented in the table below.

Summary of risk assessment for professional operators

Product (pest controlled)	**Margins of Exposure (MOE) [a]**			
	Gloves are worn		**Gloves are not worn**	
	Based on default values	**Based on measured values**	**Based on default values**	**Based on measured values**
Product P1 (rats in sewers)	249	2614	25	261
Product T P1 (rats in/around buildings and waster dump perimeters)	412	2488	42	249
Product P1 (mice in/around buildings and waster dump perimeters)	613	2488	63	249
Product P1 (rats and mice in open areas)	809	2614	83	261
Product P2 (rats in/around buildings and waster dump perimeters)	8000	7813	1124	1420
Product P2 (mice in/around buildings and waster dump perimeters)	8000	12048	1124	2304
Product P2 (rats and mice in open areas)	8000	7692	1124	1389
PRODUCT P3 (rats and mice inside buildings)	454 [b]	-	70 [b]	-
	2380 [c]	-	387 [c]	-

[a] Based on the NOAEL of 0.005 mg/kg bw/day established in 11-week rat study. Assessment factor of 300 (10 extrapolation rat to human, 10 intraspecies variability and 3 for additional factor applied to all anticoagulant rodenticides). The exposure path was considered to be dermal and inhalation

[b] From HSL model (*Consumer product spraying and dusting model 2.* TNsG Human Exposure, June 2002, page 199).
[c] From BBA model (*Mixing and loading model 5.* TNsG Human Exposure, June 2002, page 137).

The exposure path was considered to be dermal and inhalation

Human health risk for non professional users

Product P1 and Product P2 are used by non-professional on a single occasion and not on a daily basis. The use of sachets reduces exposure. Product P3 is not used by non-professionals. High margins of safety exist for non-professional operators applying both Product P1 and Product P2. The margin of exposure were much higher than 300 (the adopted assessment factor) when used for either rats or mice based either on default values or measured values (see of Table Summary of risk assessment for non-professional operators). In conclusion, the risk to non-professional users handling all products containing chlorophacinone is considered to be small, even based on worst-case values. A summary of the risk assessment for non-professional operators is presented in the table below.

Summary of risk assessment for non-professional operators

Product (pest controlled)	**Margins of Exposure [a]**	
	Gloves are not worn	
	Based on default values	**Based on measured values**
Product P1 (rats)	1225	5618
Product P1 (mice)	1815	5618
Product P2 (rats)	21505	74074
Product P2 (mice)	21505	111111

[a] Based on the NOAEL of 0.010 mg/kg bw/day established in 13 day exposure in teratogenicity rabbit study (NOAEL=0.010 mg/Kg bw/day. Assessment factor of 300 (10 extrapolation rat to human, 10 intraspecie variability and 3 for additional factor applied to all anticoagulant rodenticides. The exposure path was considered to be dermal and inhalation

The exposure paths ware considered to be dermal and inhalation.

Human health risk from indirect exposure as a result of use

Adults or children may be present following application and may theoretically be incidentally exposed by touching unprotected Product P1 and Product P2 baits. For products applied in bait stations or outdoors, incidental exposure will be very limited. Children are potentially the group most at risk as they may play inside or around buildings where baits have been placed. However, product labels and good practice advise users to prevent access to bait by children. In theory, infants could be exposed orally by chewing bait or touching their mouths with contaminated fingers. However, Product P1 and Product P2 contain a bittering agent (denatonium benzoate) to prevent oral consumption. Adults and children may occasionally be exposed to dead rodents that have been treated with Product P3.

Compared to the NOAEL of 0.010 mg/kg bw/day, the margin of exposure was 200, something lower than 300 for infants based on a default exposure value which assumes that infants will

ingest 10 mg poison bait. If children ingest 5 g poison bait, the margin of exposure was 0.4. Nevertheless, considering that default exposure scenario is using worst case approximation, considering that an extra factor is applied, considering that NOAEL is based on maternal effect in several day repeated dose, and considering that bitter compound is added to the product that reduce intake in realistic scenarios, this can be considered a rather conservative approach. It is concluded that for a single exposure, the risk attributed to the use of use of PRODUCTS P1 and P2 is considered to be acceptable. Exposure of adults and children handling dead rodents is assumed to be low.

. Table 12.3-1 Summary of risk assessment for <u>non-users for PRODUCTS P1 and P2, by oral intake</u>

Non users: assessment based on measured values				
Workplace operation	**Exposure path**	**Total systemic dose (mg/kg bw/day)**	**Repeated dose Toxicity**	
			Systemic NOAEL (mg/kg bw/day)	**MOE [a]**
In sewers, waste dump perimeters and open areas for control of rats and mice.	None. (Non-users will not be present during or after application)	–	–	–
In and around buildings for control of rats and mice.	Non-users will not be present during application. Infants may ingest part of wax blocks: **10 mg**.	0.00005	0.010	200
In and around buildings for control of rats and mice.	Non-users will not be present during application. Infants may ingest part of wax blocks: **5 g**	0.025	0.010	0.4

Regarding Product P3, compared to the NOAEL of 0.010 mg/kg bw/day, the margins of safety were considered of concern (17 and 4 for adults and children, respectively) based on default exposure values which assume that adults and children will handle dead rodents. Hence, chlorophacinone in product P3 showed an unacceptable risk for non users. Therefore, risk mitigation measures should be employed to further reduce the risk to non-users. The following can be proposed:

- Use by professionals only.
- Use this product only when the use of a traditional rodenticide bait is not suitable (e.g. where there are abundant natural foods that could reduce traditional bait take). Never use in areas where children or pets can have access.
- Before use, wear gloves, suitable protective clothing and a dust filtering respirator.
- Do not apply where draughts are considered likely to disperse the powder.
- Take care to cover or to protect the areas of powder application with tiles, baits stations, piece of wood, etc., so that they are not accessible to, or consumed by non target animals.
- If used in a non-industrial area (e.g. in farm buildings), where domestic animals may come into contact with dead rodents, the use of notices warning humans to keep domestic animals from treated areas should be considered.
- Dispose of dead rodents according to local regulation. As the bodies may have powder on the fur, the use of gloves is recommended when collecting bodies (as rodents are known disease vectors, gloves should always be worn when handling dead rodents).

Summary of risk assessment for non-users, by dermal exposure

Product	**Margins of Exposure based on default values**		
	Acute toxicity (NOAEL = 0.010 mg/kg bw/day)		
	adults (60 kg)	**children (15 kg)**	**infants (10 kg)**
Product P1 and P2 In sewers, waste dump perimeters and open areas for control of rats and mice (Non-users will not be present during or after application)	NA[a]	NA[a]	NA[a]
Product P1 and P2 In and around buildings for control of rats and mice. (Non-users will not be present during application. Infants may ingest part of wax blocks.	NA[a]	NA[a]	NA[a]
Product P3	17	4	NA[b]

[a] Not applicable. Exposure of adults and children handling dead rodents is assumed to be low.
[b] Not applicable. Product is used in areas with restricted access only to prevent exposure.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Chlorophacinone has been evaluated for its use as a rodenticide in the formulated products Product P1 (wax blocks 0.005%), Product P2 (grain baits 0.005%) and Product P3 (tracking powder 0.2%) in some of these four scenarios: Sewers, In and around buildings, Open areas and Waste dumps or landfills. Chlorophacinone is used for the urban and agricultural control of rodents indoors (i.e. in grain silos, warehouses), in and around farms buildings, waste dumps/landfills and in sewers. It is used to protect human food and animal feedstuffs and for general hygiene purposes. Chlorophacinone is released into the environment during the application processes, its service life and disposal stages. Aquatic and terrestrial compartments are affected by the emissions of chlorophacinone.

Aquatic compartment.- Chlorophacinone is not biodegradable under environmentally relevant conditions or expected to be biodegradable during sewage treatment processes. In the environment, chlorophacinone is not readily biodegradable according to the conditions of test OECD 301F (manometric respirometry test). The notifier assumed chlorophacinone to be not inherently biodegradable and also that it is not likely to be biodegradable in biological sewage treatments either under aerobic or anaerobic conditions.

Chlorophacinone exhibited little hydrolytic degradation under sterile aqueous conditions (pH~4, 7 and 9) at temperatures up to 70°C. Chlorophacinone is therefore, considered stable to hydrolysis with a $DT_{50\ hydrolysis}$ value equivalent to > 1 year at environmentally relevant temperatures. Hydrolytic degradation is not expected to be a significant process in the environment. In relation to photolysis of chlorophacinone, under artificial sunlight it was rapid in buffer solution and pond water. Chlorophacinone is photolysed with a calculated (for natural sunlight) half-life of chlorophacinone in water of 1.3 and 2.2 days for pond water (pH~8.4) and buffer water (pH~7) at 25ºC, respectively.

The adsorption/desorption screening test showed a Freundlich soil sorption coefficient normalised for organic carbon content (K_{oc}) of 136,000 to 15,600. This result indicates that chlorophacinone adsorbs strongly to soil. The log n-octanol-water partition coefficient (log K_{ow}) is a measure of the hydrophobicity of a chemical. As such, log K_{ow} is a key parameter in the assessment of environmental fate. Estimations of the K_{oc} based on the K_{ow} applying (Q)SARs for soil and sediment would be several orders of magnitude lower than the experimental value retrieved in the adsorption/desorption screening test. The drastic difference reflects that other processes are involved apart from lipophilicity. As a conclusion, adsorption to soil does not depend only on the organic carbon content. Chlorophacinone has a log P_{ow} = 2.42 (pH~7 at 23ºC), as it is below 3 it is an accepted indication of very low bioaccumulation potential. This compound will not accumulate in tissues of organisms. Measurements of aquatic bioaccumulation of chlorophacinone have not been performed. Therefore the bioconcentration factor for fish has been calculated according to the TGD, showing no potential for bioaccumulation: BCF_{fish} = 22.75 l/kg.

Atmospheric compartment.- The estimated half-life for the hydroxyl reaction in air is 14.3 hours. Furthermore, the vapour pressure of chlorophacinone as determined by OECD guideline no. 104 is $4.76 \cdot 10^{-4}$ Pa (22.8°C) and Henry's law constant is 0.013725 $Pa.m^3.mol^{-1}$

(based on a water solubility of 13.0 mg a.s/l). Therefore chlorophacinone is not expected to volatilise to air in significant quantities. In conclusion, significant amounts of chlorophacinone are not likely to volatilise or persist in air.

Soil compartment.- Biotic degradation in soil: In soil under dark aerobic conditions in the laboratory (12°C (European mean temperature) extrapolated from 25°C), chlorophacinone is degraded steadily with an estimated DT_{50} value of 128 days. Degradation of chlorophacinone did not lead to the formation of any significant metabolites (i.e. > 10% AR). Several minor metabolites (i.e.< 10% AR) were observed. Degradation of chlorophacinone results predominantly in the formation of carbon dioxide (61.0% AR after *ca* 100 days) (mineralization). Metabolites (including o-phthalic acid and p-chlorophenyl phenyl acetic acid) do not exceed 10% AR at any sampling interval. Soil non-extractable residue (NER) comprises 9.0% AR after *ca* 100 days. chlorophacinone quickly photo-degraded on a soil surface when exposed to an artificial light source, with an equivalent DT_{50} value of 11.1 days (12°C). Degradation of chlorophacinone resulted in the formation of a major metabolite o-phthalic acid (37.1% AR), carbon dioxide (potentially 50% AR) and three minor degradation products (< 10% AR).

2.2.2.2. Effects assessment

Aquatic compartment (including STP and sediment)

In the absence of any long-term toxicity endpoints and with at least one short-term $L(E)C_{50}$ from each of three trophic levels of the base set (fish, daphnia and algae), the Risk Assessment TGD prescribes an assessment factor of 1000. Based on the lowest acute endpoint of LC_{50} (96h) = 0.45 mg chlorophacinone/l for *O. mykiss*, the surface water $\mathbf{PNEC_{aquatic}}$ is $0.45/10^3 = \mathbf{4.5 \cdot 10^{-4}}$ **mg a.s/l**.

According to the TGD (ECB Part II, 2003), the PNEC for microorganisms in a STP is derived by dividing the NOEC or EC_{10} from a respiration inhibition test (OECD 209) by a factor of 10. In this case the NOEC has been established from an EC_{15} but it can also be considered a NOEC. The EC_{15} (3 h) of chlorophacinone was determined at 775 mg/l in a static test with activated sludge. It has to be taken into account that this value is far above the water solubility limit. $PNEC_{microorganisms}$ will be derived from the water solubility 344 mg a.s/l (pH~7, 20ºC) and an AF of 10. $PNEC_{microorganisms}$ = 34.4 mg a.s/l.

In the absence of any ecotoxicological data for sediment-dwelling organisms and due to the fact that for chlorophacinone it is not possible to use the partitioning method (because of the uncertainty shown by the K_{oc} estimation based on its K_{ow}) the $PNEC_{sed}$ can not be calculated.

Terrestrial compartment

The acute LC_{50} of chlorophacinone to the earthworm *E. foetida* is greater than 1,000 mg a.s/kg dry soil. According to the Risk Assessment TGD, since this endpoint was obtained in a study that used OECD artificial soil containing 10% organic matter, it requires normalisation to represent a "standard" natural soil with an average organic matter content of 3.4%: $LC_{50\ standard\ soil}$ (>1000 × (3.4/10)), *i.e.* >340 mg chlorophacinone/kg dry soil > 300 mg a.s/ kg wwt soil. Conversion factor = 1.13 $kg_{wwt} \cdot kg_{dwt}^{-1}$ (from EUSES 2.0)

No data have been provided for plants and no evidences exists for considering them less sensitive than earthworms. According to TM's decision no test on terrestrial plants will be requested and an AF of 1000 will be applied. **$PNEC_{soil}$ is > 0.30 mg chlorophacinone/kg wwt soil**. For chlorophacinone, it is not possible to calculate the $PNEC_{soil}$ using the partitioning method due to the uncertainty in the binding mechanism shown by the discrepancies between the measured K_{oc} and the value estimated from the K_{ow}.

Non compartment specific effects relevant to food chain (primary and secondary poisoning)

Having checked the two studies on absorption, distribution, metabolism and excretion performed with chlorophacinone in rats where it is assumed that most of the active substance is excreted, and acknowledging that chlorophacinone has a log P_{ow} = 2.42 (pH~7 at 23ºC); value below 3, it is accepted that chlorophacinone has a low potential to bioaccumulate. No studies on the bioconcentration potential of chlorophacinone in aquatic and terrestrial environment have been supply by the applicant to confirm its low bioaccumulation potential.

Mammals. Primary poisoning. The most sensitive organism is the rat in the subchronic oral test (11 to 16 weeks) with a NO(A)EL of 0.005 mg a.s/kg bw. The RMS proposed the derivation of a threshold value expressed as dose (mg a.s/kg bw) as substitute of the PNEC following the current state of the art and recommendations from several EU Scientific Committees; however, at the TM, it was decided to request the RMS to change the assessment and to follow strictly the approach adopted for other rodenticides. The RMS considers that the application of the TGD proposal to rodenticides requires a scientifically based adaptation, and in the estimation of a NOEC in mg a.s./kg food from a non-dietary test (the NOAEL is from a gavage administration study) does not follow the TGD principles, but the opinion of the RMS was not accepted by the TM. Therefore, the calculations presented below do not present the proposal of the RMS but the decision adopted at the TM. According to the TM, the NOAEL must be transformed into a NOEC using a TGD factor of 20, and the AF_{oral} of 90 should be applied to this NOEC. Taking these explanations into account the PNEC for mammals is:

$PNEC_{mammals}$ = (0.005 x 20)/90 = **0.0011 mg a.s/kg food**

It should be noticed that the PNEC expressed as mg a.s/kg food should not be extrapolated among species with different food intake ratios. According to the calculations conducted by the RMS (see complementary document produced by Spain. Suárez E. *et al*., 2008. Assessing the environmental risk for primary and secondary poisoning in birds and mammals of the rodenticide chlorophacinone. INIA-MMAMRM report. July 2008) this $PNEC_{mammals}$ of 0.0011 mg a.s./kg food should be applied to species and individuals with a food intake ratio of about 0.15 (ingestion of up to 15% of their body weight as food per day).

The qualitative assessment agreed upon in the TM has been included as a first step in assessing the acute risk, but it did not provide conclusive evidences. Thus, a quantitative proposal has been developed by the RMS and presented as an annex in document IIC. The NO(A)EL of 0.005 mg a.s/kg bw has also been used for those long-term estimations which according to EUBEES 2 require the use of toxicity endpoints expressed as dose. In addition to the direct comparison, a tentative Estimated No Effect Level (ENEL) has been derived following rhe

principles established in the TGD and risk quotients have been presented as supporting information.

The relevancy of the acute risks has been confirmed from incidents occurred last February 2007 in Spain due to the direct application by farmers of a formulation based on chlorophacinone registered as a pesticide product in Spain. The RMS considers that the inclusion of an acute quantitative approach for the comparative risk assessment is very relevant.

Birds. Primary poisoning. Based on the 5-day dietary LC_{50} study, in Bobwhite quail (*Colinus virginianus*), LC_{50} is 95 mg a.s/kg food (AF_{oral} of 3,000). **$PNEC_{birds}$ = 0.03 mg a.s/kg food**.

2.2.2.3. PBT assessment

The available data are sufficient for a PBT assessment of chlorophacinone. Chlorophacinone can be classified as not readily biodegradable, and it is considered stable to hydrolysis at environmentally relevant temperatures hence, the screening criteria for persistence is met. Rapid photolysis in water: DT_{50} (25ºC) = 2.2 d; pH~7, and soil. DT_{50} (12ºC) = 11.1 d are reported. Degradation studies are reported for soil $DT_{50\ lab\ soil}$ (20ºC) = 47.3 days , but not for water-sediment or freshwater, thus a definitive assessment of the P criteria cannot be established. The log P_{ow} = 2.42 (pH~7; 23ºC) indicating low potential for bioaccumulation. The substance does not fulfil the B criterium. In conclusion, since chlorophacinone does not meet criteria B, it is not considered a PBT candidate.

2.2.2.4. Exposure assessment

2.2.2.4.1. Product P1 and Product P2 (wax blocks and grain baits, 0.005%)

Product P1 (0.005%) are red solid, neutral, blocks (ready for use) with grain seeds visible on the surface and a grain/wheat odour. Exposure to the primary receiving environmental compartments, water, air and soil depends on the physico-chemical properties of the substance as well as its formulation type, mode of application, use and disposal.

Environmental compartments of concern for a chlorophacinone rodenticide wax block bait formulation such as Product P1 (0.005%)

Environmental compartment of concern	Exposure scenarios			
	Sewers	In and around buildings	Open areas	Waste dumps
Use	Professional	Non/professional	Professional	Professional Only perimeters
Target organism	*Rattus norvegicus*	*Rattus norvegicus*	*Rattus norvegicus*	*Rattus norvegicus*
STP	√	-	-	-
Surface water	√	-	-	-
Sediment	Not quantificable	-	-	-
Soil	not quantificable	√	√	√
Ground water	No specific scenario for biocides developed			
Air	-	-	-	-
Primary poisoning	-	√	√	√
Secondary poisoning	√	√	√	√

Product P2. Grains (baits, used as supplied) ready-to-use containing the active substance chlorophacinone are used in areas in and around buildings, open areas and waste dumps. Grain products can be supplied with (professional and amateur) and without sachets (professional only). A control campaign could last for approximately 21 days. After the control campaign has finished, all the product not consumed is collected and disposed of safely. During the visits to bait points any dead rodents visible are collected for disposal.

Environmental compartments of concern for a chlorophacinone rodenticide red grain bait formulation such as Product P2 (0.005%)

Environmental compartment of concern	Exposure scenarios		
	In and around buildings	Open areas	Waste dumps
Use	Non/professional	Professional	Professional Only perimeters
Target organism	*Rattus norvegicus* and *Mus musculus*		
STP	–	–	-
Surface water	–	–	-
Sediment	-	-	-
Soil	√	√	√
Ground water	No specific scenario for biocides developed		
Air	-	-	-
Primary poisoning	√	√	√
Secondary poisoning	√	√	√

A control campaign could last for approximately 21 days. After the control campaign has finished, all the product not consumed is collected and disposed of safely. During the visits to bait points any dead rodents visible are collected for disposal.

An environmental exposure assessment has been conducted based on the fate and distribution properties of the active substance, chlorophacinone, as determined from laboratory studies. The

potential predicted environmental concentration (PEC) of chlorophacinone has been estimated, where appropriate, in various environmental compartments (surface water, groundwater, sediment, air and soil) following realistic worst case and, where appropriate, normal case usage scenarios. Only local PECs are used since regional and continental releases are regarded to be negligible.

PEC in surface water, groundwater, STP and sediment.-

Sewers: If unused product, urine or excreta from target rodents or dead rodents enter the sewage system, chlorophacinone may reach surface waters via the final effluent discharged from a sewage treatment plant (STP). Estimates of chlorophacinone concentrations in surface water that arise from this application in a realistic worst case situation were calculated giving a PEC in the STP of $9.6 \cdot 10^{-5}$ mg a.s/l and a $PEC_{surface\ water}$ of $9.6 \cdot 10^{-6}$ mg a.s/l in the first week.

The partitioning method for the calculation of $PEC_{sediment}$ is not considered appropriate due to the high discrepancies between the measured K_{oc} and the K_{oc} derived from the K_{ow}. No measured K_{oc} sediment data are available, thus, no quantitative risk characterisation for sediment can be performed. However, the assessment conducted for the aquatic compartment will also cover the sediment compartment. $PEC_{sediment}$ can not be estimated since the fraction that adheres to the organic matter is unknown due to the uncertainties in the procedures involved in the partitioning of the substance. This means that it is not possible to know the way it is distributed between the different compartments since other processes apart from adhesion to organic matter take place unabling the estimation of the percentage that does not lixiviate.

Based on the physico-chemical properties and uses of chlorophacinone in sewers, groundwater contamination is not expected to occur. The relative distribution of chlorophacinone in sludge which may eventually reach soil will be very low. Furthermore, due to the relative adsorption ($K_{oc} \geq 15{,}600$ ml/g) to soil the likelihood for groundwater contamination is low.

In and around buildings (applies also to product P2): Chlorophacinone is not expected to appear in surface waters at significant concentrations (EUBEES 2) following the use of bait blocks/grains in and around buildings. Therefore, PEC values for chlorophacinone in surface water and sediment are assumed to be negligible and have not been further considered.

$PEC_{groundwater}$ has been calculated, as requested by TM, for indirect exposure of humans through drinking water. According to TGD this is a worst-case assumption, neglecting transformation and dilution in deeper soil layers and in addition the calculations assume a regional application of the product, what is not true for rodenticides leading to an unrealistic estimation. The highest concentration in soil is for products P1 and P2 in open areas 0.17 mg a.s/kg wet soil and this has been the quantity used in the calculations. $PEC_{local\ gw} = PEC_{local\ agr,\ soil,\ porew} = 0.0006$ µg a.s/l < 0.1 µg a.s/l.

The RMS considers that the use of a scenario such as the one from EUSES or FOCUS is not reasonable due to the fact that those assume soil to be contaminated, regional approach, representative for several hectares (Ha) and not a few cm^2. A scenario with a local approach for biocides should be developed. Nevertheless, the unrealistic worst case estimation indicates concentrations below the threshold for chlorophacinone.

Open areas and waste dumps (applies also to Product P2): Chlorophacinone is not expected to appear in surface waters at significant concentrations (EUBEES 2) following the use of bait blocks/grains in open areas. Therefore, PEC values for chlorophacinone in surface water and sediment are assumed to be negligible and have not been further considered. Please see In and Around buildings

PEC in atmosphere (applies also to product P2 and P3).-

The vapour pressure of chlorophacinone at ambient temperature is 4.76×10^{-4} Pa (OECD 104). Chlorophacinone is, therefore, not considered volatile and is not expected to volatilise to air in significant quantities following use in any of the usage scenarios (i.e. sewers, in and around buildings, open areas and waste dumps, where relevant). In addition, the photochemical oxidative degradation half-life of chlorophacinone in air has been estimated using the Atmospheric Oxidation Program v1.90 (AOPWIN), which is based on the structural activity relationship (QSAR). The half-life for the hydroxyl reaction in air is estimated to be 14.3 hours, indicating that if present in air, chlorophacinone would not be expected to persist. Chlorophacinone is not expected to volatilise to or persist in air in significant quantities; consequently, the potential concentration of chlorophacinone in air is considered to be negligible.

PEC in the terrestrial compartment.-

The PECs of chlorophacinone in soil arising from the various usage scenarios (sewers, in and around buildings, open areas and waste dumps) are considered. Exposure to soil may also arise from the use of sewage sludge in agriculture. However, exposure arising from this application is considered to be covered by the other scenarios (in and around buildings, open areas and waste dumps) since their pattern of use could potentially lead to the highest concentration of active substance in soil.

Sewers (only Product P1): Direct contamination of soil following the use of bait blocks in sewers is highly unlikely during application and use. Surplus STP sludge may be applied to soil as a fertiliser and indirect contamination of soil may occur if a substance with a high affinity for organic matter resists breakdown during anaerobic treatment and is still bound to the sludge at the time when it is applied. Since it is not possible to know the percentage that would adsorb to sludge, a quantitative estimation of the concentration in soil is not possible. Air-stripping is not expected to occur and subsequent aerial transport and air-to-ground deposition are therefore not relevant for chlorophacinone.

In and around buildings (applies also to Product P2): Exposure of the terrestrial compartment (soil) will occur when bait blocks are deployed outdoors. EUBEES 2 considers a scenario that entails outdoor baiting with blocks around a farm building. In this situation, exposure is assumed to arise through a combination of transfer (direct release) and deposition via urine and faeces (disperse release) onto soil. Direct release is estimated to amount to 1.0% of the total bait deployment during the entire campaign, concentrated within 10 cm of the individual secured bait points. Similarly, EUBEES 2 considers that 90% of the total amount of rodenticide consumed by the target rodents over the duration of the outdoor baiting campaign enters soil via urine and faeces. In this case the total exposure area is 330 m^2.

The local predicted environmental concentration in soils is equivalent to the local soil concentration as for rodenticides the consumption is estimated to be so low that the regional contribution is negligible (PT 14 ESD p.13). Hence $PEClocal_{soil}$ (initial) = $C_{local\ soil}$. $PEC_{local\ soil\ RWC}$ = 0.019 mg a.s/kg soil and $PEC_{local\ soil\ normal\ situation}$ = 0.005 mg a.s/kg soil.

Open areas (applies also to Product P2): Bait blocks are applied in open areas by placing them inside the tunnel openings of the target rodents and, according to the scenario presented in EUBEES 2, two such treatments would typically be applied in the space of six days. Product is deployed in burrows, 3 x 30 g blocks per application per burrow on typically two occasions. Based on a tunnel of 8 cm diameter, worst-case soil exposure is assumed to occur to a depth of 10 cm from the contact half (*i.e*. the burrow floor) of a 30 cm tunnel section in which the bait is placed. This section of tunnel floor is assumed to receive an input corresponding to 5% of the product during application and a further 20% as the bait is consumed. $PEC_{local\ soil\ RWC}$ = 0.16 mg a.s/kg soil.

Waste dumps (also applies to Product P2): Bait blocks are deployed around the perimeter of waste-dumps and land-fill sites to control populations of rats. EUBEES 2 suggests a worst-case scenario in the event of an infestation outbreak that entails 40 kg of blocks protected inside bait boxes distributed over an area of 1 ha, with a total of seven such applications per year. In this situation, soil exposure is assumed to arise through a combination of deposition via urine and faeces plus the rodenticide contained in the carcasses of poisoned target rodents. Ninety percent of the total amount of rodenticide consumed by the target rodents over the duration of each baiting campaign is assumed to enter soil over the 1 ha surface. $PEC_{local\ soil\ RWC}$ = 0.007 mg a.s/kg soil.

2.2.2.4.2. Product P3 (tracking powder, 0.2%)

Product P3 (0.2%) is a blue tracking powder (ready to use), used inside buildings such as houses, animal houses, commercial and industrial sites in cracks or cavities. The product is not used routinely, but in emergency situations in limited quantities (four points per room of 25 g P3, two rooms per day) where rodent populations are very high and where competition for food makes control with baits impractical or inappropriate. The product is only used in response to an infestation. The product is ingested when the rodents groom themselves. Application of chlorophacinone tracking powder is confined to indoor rodent control. The product is only applied by trained professional users. Target organisms are *Rattus norvegicus* and *Mus musculus*.

Environmental compartments of concern for a chlorophacinone rodenticide tracking powder formulation such as Product P3 (0.2%).

Environmental compartment of concern	Exposure scenarios
	Inside buildings
Use	Professional
Target organism	*Rattus norvegicus* (Norway rat, Brown rat) *Mus musculus* (House mouse)
STP	-
Surface water	-
Sediment	-
Soil	-
Groundwater	No specific scenario developed for biocides
Air	-
Primary poisoning	√
Secondary poisoning	√

These use patterns have been employed for developing a tentative risk assessment.
No exposure scenarios are currently available for this specific use. Thus, a case-specific approach is presented. The information is not sufficient for presenting a quantitative estimation, nevertheless, a qualitative assessment and some preliminary comparisons between toxicity and the expected exposure level are presented.

PEC in surface water, groundwater, STP and sediment

Inside buildings (Product P3)

Due to use patterns (holes and burrows within buildings) releases to water bodies are considered negligible if the trained professional applicators follow the use pattern conditions.

PEC in the terrestrial compartment

Inside buildings (Product P3)

Due to use patterns (holes and burrows within buildings) releases to soil are considered negligible if the trained professional applicators follow the use pattern conditions.

NON COMPARTMENT SPECIFIC EXPOSURE RELEVANT TO THE FOOD CHAIN (PRIMARY AND SECONDARY POISONING).-

Please see 2.2.2.5. Risk characterisation **(applies to P1, P2 and P3)**.

2.2.2.5. Risk characterisation

2.2.2.5.1. Risk characterisation for Products P1 and P2.

STP, aquatic compartment (including sediment) and groundwater.-

Sewers (Product P1, wax blocks 0.005%)

Exposure scenario	PEC (mg a.s/l)	PNEC (mg a.s/l)	PEC/PNEC
STP (RWC, first week)	$9.6 \cdot 10^{-5}$	34.4	$2.8 \cdot 10^{-6}$
Surface water (RWC, first week)	$9.6 \cdot 10^{-6}$	0.00045	0.02

Regarding risk characterisation for STP and surface water, PEC/PNEC values were below 1.

$PEC_{sediment}$ can not be estimated since the fraction that adheres to the organic matter is unknown due to the uncertainties in the procedures involved in the partitioning of the substance. This means that it is not possible to know the way it is distributed between the different compartments since other processes apart from adhesion to organic matter take place unablingnot allowing the estimation of the percentage that does not lixiviate.

In and around buildings (products P1 and P2, grain bait 0.005%)

Chlorophacinone is not expected to occur to appear in surface waters at significant concentrations any significant extent in surface waters (EUBEES 2) following the use of bait blocks in and around buildings. Therefore, PEC values for chlorophacinone in surface water and sediment are assumed to be negligible and have not been further considered.

$PEC_{groundwater}$ has been calculated, as requested by TM, for products P1 and P2. $PEC_{local\ gw}$ = $PEC_{local\ agr,\ soil,\ porew}$ = 0.0006 µg a.s/l < 0.1 µg/l.

Open areas and Waste dumps (Products **P1 and P2)**

Chlorophacinone is not expected to appear in surface waters at significant concentrations (EUBEES 2) following the use of bait blocks in and around buildings. Therefore, PEC values for chlorophacinone in surface water and sediment are assumed to be negligible and have not been further considered.

Atmosphere.- (Products P1, P2 and P3)

The estimated half-life for the hydroxyl reaction in air is 14.3 hours. Furthermore, the vapour pressure of chlorophacinone as determined by OECD guideline no. 104 is $4.76 \cdot 10^{-4}$ Pa (22.8°C) and Henry's law constant is 0.013725 $Pa.m^3.mol^{-1}$ (based on a water solubility of 13.0 mg/l). Therefore chlorophacinone is not expected to volatilise to air in significant quantities. In conclusion, significant amounts of chlorophacinone are not likely to volatilise or persist in air.

Terrestrial compartment.-

Sewers (Product P1)

Exposure to soil may also arise from the use of sewage sludge in agriculture. However, exposure arising from this application is considered to be covered by the other scenarios (in and around buildings, open areas and waste dumps) since their pattern of use could potentially lead to the highest concentration of active substance in soil.

Exposure of the terrestrial compartment is considered to be negligible and the risks presented to terrestrial biota by chlorophacinone deployed in sewers are expected to be very low. No further assessment of risk is necessary.

In and around buildings (Products P1 and P2)

As stated above, the “typical” pattern is the one more likely to apply to an efficient anticoagulant rodenticide such as chlorophacinone. However, the PEC/PNEC ratios based on the maximum PEC that represent “hotspots” of contamination surrounding each bait point are less than 1. No test on plants has been requested according to TM’s decision.

Baiting scenario (EUBEES 2)	PEC_{soil} (mg a.s/kg wwt)	$PNEC_{soil}$ (mg a.s/kg wwt)	PEC/PNEC
Realistic worst-case	0.019	> 0.30	< 0.06
Typical	0.005	> 0.30	< 0.02

Open areas (Products P1 and P2)

The PEC/PNEC ratio based on the PEC that represents a localised "hotspot" of contamination near the entrance of each baited tunnel is less than 1.This case is a confirmatory example of the necessity of performing a short-term toxicity test to plants. Since if plants were to be twice more sensitive to chlorophacinone than earthworms, this PEC/PNEC ratio for soil would become equal or higher than 1 posing a risk for soil-dwelling organisms in open areas.

Baiting scenario (EUBEES 2)	PEC_{soil} (mg a.s/kg wwt)	$PNEC_{soil}$ (mg a.s/kg wwt)	PEC/PNEC
Worst-case	0.16	> 0.30	< 0.53

Waste dumps (Products P1 and P2)

The PEC/PNEC ratio is less than 1 under the worst case conditions suggested by EUBEES 2.

Baiting scenario (EUBEES 2)	$PEC_{local\ soil}$ (mg chlorophacinone/kg wwt)	$PNEC_{soil}$ (mg chlorophacinone/kg wwt)	PEC/PNEC
Worst-case	0.007	> 0.30	< 0.02

Non compartment specific effects relevant to food chain (primary and secondary poisoning).- (Products P1 and P2)

The RMS considered the information included in the dossier and obtained from a field episode for producing a higher tier risk assessment. Nevertheless, at the TM it was agreed that for harmonization purposes the risk assessment should be conducted following a similar procedure than that employed for other rodenticides and requested the RMS to modify the assessment. Thus, the assessment included here does not represent the RMS proposal but the TM decision. The assessment presented here following the TM recommendations is exclusively intended for decision-making under the Biocides Directive. The RMS has produced a higher tier assessment, containing information that could be valuable for site-specific assessments and diagnosis purposes which is available as a complementary document (Suárez E. et al., 2008. Assessing the environmental risk for primary and secondary poisoning in birds and mammals of the rodenticide chlorophacinone. INIA-MMAMRM report. July 2008).

The exposure of chlorophacinone directly to non-target birds and mammals (primary poisoning) and indirectly via target rodent carcasses (secondary poisoning) is considered a critical aspect of the risk assessment. A qualitative assessment agreed upon in the TM has included as a first step in assessing the acute risk.

The qualitative approach for the acute situation confirms the potential risk of primary poisoning to dogs. The level of the risk is not clarified for all other species with this approach, as an ETE below the LD_{50} does not indicate the absence of unacceptable risk if the required margin of safety is not established. As a consequence, the RMS has developed an acute approach for chlorophacinone which could be used for the purpose of the comparative risk assessment of second generation anticoagulants after product authorisation (annex in document II C).

Sewers (Product P1)

Primary poisoning: Exposure scenario not considered relevant in the EUBEES 2 ESD for rodenticides. Section 2.3.4. of EUBEES 2: "There is no primary poisoning hazard to mammals or birds because no other mammals (or birds) are living or occurring in sewers".

Secondary poisoning: It is unlikely that target rodents that have eaten bait blocks containing chlorophacinone will leave the sewer system and be exposed, in significant numbers, to predators or scavengers (if that was not the case, the situation would be similar to the one described below for in and around buildings).

In and around buildings (Products P1 and P2)

Primary poisoning:

Basically the same set of physiological processes is responsible for maintaining life for warm-blooded animals, i.e. mammals and birds. Therefore, the use of rodenticides meant for killing selected pest mammals has to be considered a general hazard to non-target mammals and birds as well.

Primary poisoning, qualitative approach. Tier 2, single uptake (short-term exposure). Mammals and birds.-

Regarding the qualitative assessment only a description of the toxicity of the substance compared to the possible single uptake is presented instead of carrying out a quantitative risk assessment. It is important to stress that this qualitative assessment is a simple comparison of the acute exposure situation with single dose LD_{50} values. The qualitative risk assessment is not intended to be used for risk characterisation; no $PNEC_{oral}$ shall be derived and hence no PEC/PNEC ratio can be established. This comparison should only give a first indication of the acute toxicity of the substance. This qualitative assessment is not intended to be used for the risk characterisation of primary and secondary poisoning of rodenticides and shall not be used for a comparative assessment.

Tier 2. Primary poisoning qualitative assessment. Expected content of the active substance chlorophacinone in non-target animals (mammals) in the worst case situation, following the EUBEES-ESD (concentration of a.s. in rodenticide wax block 0.0050%). Short-term exposure (single uptake. Acute effects). Product P1 and P2.

Organism	Species	Body weight (g)	Daily mean food intake (g)	Bait consumption (g product)	Estimated daily uptake of chlorophacinone, ETE (mg a.s/kg bw)	
					First tier*	Second tier*
Dog	*Canis familiaris*	10,000	-*	600.0	**3.0**	**2.2**
Pig	*Sus scrofa*	80,000	-*	600.0	0.4	0.3
Pig, young	*Sus scrofa*	25,000	-*	600.0	1.2	0.9
* Not stated in the EUBEES-ESD; simplistically, a maximum bait consumption of 600 g is assumed in rodenticide bait 0.005%						

*First tier (worst case) AV=1, PT =1; Second tier (realistic worst case) AV=0.9, PT=0.8. Corrected for a maximum ingestion of 600 g bait.

The lowest acute endpoint is for dog LD_{50} « 2 mg a.s/kg bw. Making the comparison between the ETE, only dogs present a higher exposure than the toxicological endpoint. For the rest of the mammals the level of the risk not clarified with this approach, as an ETE below but close to the LD_{50} does not indicate the absence of unacceptable risk.

Tier 2. Primary poisoning qualitative assessment. Expected content of the active substance chlorophacinone in non-target animals (birds) in the worst case situation, following the EUBEES-ESD (concentration of a.s. in rodenticide wax block 0.0050%). Short-term exposure (single uptake. Acute effects). Products P1 and P2.

Organism	Species	Body weigh t (g)	Daily mean food intake (g food/d)	Bait consumption (g product)	First tier*		Second tier*	
					ETE** mg a.s./kg bw	PEC mg a.s/kg food	ETE mg a.s/kg bw	PEC mg a.s/kg food
Tree sparrow	*Passer montanus*	22	7.6	7.6	17.3	50	12.4	36
Chaffinch	*Fringilla coelebs*	21.4	6.42	6.42	15.0	50	10.8	36
Wood pigeon	*Columba palumbus*	490	53.1	53.1	5.4	50	3.9	36
Pheasant	*Phasianus colchicus*	953	102.7	102.7	5.4	50	3.9	36

*First tier (worst case) AV, PT and PD =1; Second tier (realistic worst case) AV=0.9, PT=0.8 and PD=1.
**ETE, Estimated daily uptake of chlorophacinone

The lowest acute endpoint is for *C. virginianus* LD_{50} = 257 mg a.s/kg bw. All ETE are below this endpoint for birds. The level of the risk is not clarified with this approach, as an ETE below the LD_{50} does not indicate the absence of unacceptable risk if the required margin of safety is not established.

Primary poisoning for mammals. Long-term exposure.-

Tier 2. Long-term risk characterisation for different primary poisoning scenarios to mammals (wax block 0.005%). Products P1 and P2.

Exposure scenario (species, $ENEL_{mammal}$)	ETE (mg a.s/kg bw)		$ETE/ENEL_{mammals}$	
	First tier*	Second tier*	First tier*	Second tier*
Dog (0.00017-0.00006 mg a.s/kg bw)	3.0	2.2	**17,647-50,000**	**12,941-36,667**
Pig (0.00017-0.00006 mg a.s/kg bw)	0.4	0.3	**2,353-6,667**	**1,765-5,000**
Pig, young (0.00017-0.00006 mg a.s/kg bw)	1.2	0.9	**7,059-20,000**	**5,294-15,000**

*First tier (worst case) AV, PT = 1; Second tier (realistic worst case) AV = 0.9, PT = 0.8. Corrected for a maximum ingestion of 600 g bait..

All ETE values are higher than the NOAEL and the tentative risk quotients arevery high (1,765-36,667 at second tier) suggesting a potential high risk. However, it should be considered that the use of a long-term PNEC is not realistic, as it assumes that the same non-target mammal must ingest the bait everyday. It is clear that at repeated doses the rodenticide poses a potential high risk to mammals, even at tier 2.

Primary poisoning for birds. Long-term exposure.-

Tier 2. Long-term risk characterisation for different primary poisoning scenarios to birds (wax block 0.005%). Product P1 and P2.

Exposure scenario Species (bw), ($PNEC_{bird}$)	PEC (mg a.s/kg food) Realistic worst case		$PEC/PNEC_{birds}$ Realistic worst case	
	First tier*	Second tier*	First tier*	Second tier*
Birds, (0.03 mg a.s/kg food)	50	36	**1,667**	**1,200**

*First tier (worst case) AV, PT and PD = 1; Second tier (realistic worst case) AV = 0.9, PT = 0.8 and PD =1.

In a long-term situation, all mammals and birds are potentially at risk of primary poisoning and mammals more than birds. To minimise the likelihood of target rodents developing resistance to anticoagulant rodenticides, long-term deployment of bait blocks as a preventative control measure is not recommended. Product labels and approved guidance on good practice additionally instruct users to retrieve and securely dispose of all unconsumed baits at the end of control programmes. Both these factors limit the opportunity for exposure and reduce the primary poisoning risk to small non-target animals. Because of the toxic nature of rodenticides it is absolutely necessary to develop and validate risk management procedures in order to minimise the risk to non target animals.

If label instructions are followed, as should be the case for normal use, the primary poisoning risk should be negligible. The assessor should check what the exposure would be if the label conditions are followed. The reason is to assure that label instructions are fully adequate to mitigate intrinsic risk that these products potentially present (ESD, EUBEES 2).

Secondary poisoning:

Quoting the EUBEES 2 guideline: “It could be argued that both an acute and a chronic risk assessment should be done for anticoagulants, because although the mode of action is generally chronic, some anticoagulants have substantial acute toxicity”.

Secondary poisoning, qualitative approach. Tier 2, single uptake (short-term exposure). Mammals and birds.-

Regarding the qualitative assessment only a description of the toxicity of the substance compared to the possible single uptake is presented instead of carrying out a quantitative risk assessment. It is important to stress that this qualitative assessment is a simple comparison of the acute exposure situation with single dose LD_{50} values. The qualitative risk assessment is not intended to be used for risk characterisation; no $PNEC_{oral}$ shall be derived and hence no

PEC/PNEC ratio can be established. This comparison should only give a first indication of the acute toxicity of the substance. It is important to stress that this qualitative assessment is not intended to be used for the risk characterisation of primary and secondary poisoning of rodenticides and shall not be used for a comparative assessment.

Tier 2 for secondary poisoning for non-target mammals containing chlorophacinone obtained from areas in and around buildings. Short-term exposure. Qualitative approach. Products P1 and P2.

Bait consumption	**$ETE_{predator}$** (mg a.s./kg predator bw)
based on residues in the rat after 5 days of ingestion after last meal	
100% normal situation Fox *V. vulpes* (5,700 g; 520.2 g food (rat in this case)/d DFI)**	0.08*
100% Polecat *Mustela putorius* (689 g; 130.9 g/d DFI)	0.18*
100% Stoat *Mustela erminea* (205 g; 55.7 g/d DFI)	0.25*
100% Weasel *Mustela nivalis* (63 g; 24.7 g/d DFI)	0.36*

* Based on a $PEC_{oral\ predator}$ of 0.93 mg a.s/kg rat bw, for a bait consumption of 100%.
** In the case of foxes in a short-term exposure situation the fraction of poisoned rodents in their diet might be below 1.

The lowest acute endpoint is for dog LD_{50} « 2 mg a.s/kg bw. All values are below the threshold of the acute endpoint (although the uncertainty in the test for dogs still remains since the endpoint value is expressed as much lower than 2 mg a.s/kg bw). The level of the risk is not clarified with this approach, as an ETE below the LD_{50} does not indicate the absence of unacceptable risk if the required margin of safety is not established.

Tier 2 for secondary poisoning for non-target birds containing chlorophacinone obtained from areas in and around buildings. Short-term exposure. Qualitative approach. Products P1 and P2.

Bait consumption	**ETE_{birds}** (mg a.s./kg predator bw)
based on residues in the rat after 5 days of ingestion after last meal	
100% Barn owl *Tyto alba* (294 g bw; 72.9 g food (rat in this case, Daily Food Intake)	0.23*
100% Kestrel *Falco tinnunculus* (209 g bw; 78.7 g DFI)	0.35*
100% Little owl *Athene noctua* (164 g bw;46.4 g DFI)	0.61*
100% Tawny owl *Strix aluco* (426 g bw; 97.1 g DFI)	0.21*

* Based on a $PEC_{oral\ predator}$ of 0.93 mg a.s/kg rat bw, for a bait consumption of 100%

The lowest acute endpoint is for *C. virginianus* LD_{50} = 257 mg a.s/kg bw. All values are below the acute endpoint. The qualitative approach for the acute situation gives no information neither for mammals nor for birds for the secondary poisoning since an ETE below the LD_{50} does not indicate the absence of unacceptable risk if the required margin of safety is not established.

Tier 2 of secondary poisoning for non-target organisms (birds and mammals with measured residues of chlorophacinone in target rodents during a field incident.-

The various concentrations of chlorophacinone in target rodents on day 5 and day 7 *pro rata* to reflect real measured residues in homogenised whole-body tissues have been used instead of the estimated values based on kinetics. Due to the incidents occurred in Spain in February

2007, a group of experts from the INIA sampled the area and collected carcasses from common voles (*Microtus arvalis*) in order to analyse residues of chlorophacinone in their bodies. Chlorophacinone was extracted and the analysis were carried out with an HPLC-mass spectrometry. The Limit Of Detection (LOD) was ≥ 20 ng/g wet weight and the Limit Of Quantification, LOQ, ≥ 30 ng/g wet weight. The concentrations found varied from the LOD up to 0.5 µg/g bw. Considering a mean weight of 20-30 g and an uniform distribution of the substance in the whole organism, the maximum quantity of rodenticide per animal would be between 10 and 15 µg chlorophacinone. These results are in line with those described in the bibliography. This incident also offered indications, not confirmed, of secondary poisoning of mammals with levels clearly much lower than those used in the EUBEES 2 guideline and similar to the ones provided by the notifier in the semifield study. The values estimated from the Spanish incident are presented below and will be used for a risk refinement under realistic field conditions.

Secondary poisoning for mammals. Tier 2. Long-term exposure.-

Exposure levels (ETE) have been estimated from the semifield studies. Even for this refined assessment, all exposure levels are higher that the rat NO(A)EL of 0.005 mg a.s/kg bw. In addition, the ETEs have been compared with the tentative Estimated No Effect Level which is presented as a range. The risk quotients (ETE/ENEL) are summarised in the table below.

Tier 2 for secondary poisoning for non-target mammals containing chlorophacinone obtained from areas in and around buildings. Long-term risk characterization. Products P1 and P2.

Bait consumption	**$ETE_{predator}$** (mg a.s./kg predator bw)	**$ENEL_{mammals}$** (mg a.s./kg predator bw)	**$ETE/ENEL_{mammals}$**
Based on residues in the rat after 5 days of ingestion after last meal			
100% realistic worst case (not for foxes**) Fox *Vulpes vulpes* (5,700 g; 520.2 g food (rat in this case)/d DFI)	0.04*	0.00017-0.00006	**235-667**
100% Polecat *Mustela putorius* (689 g; 130.9 g/d DFI)	0.08*	0.00017-0.00006	**470-1,333**
100% Stoat *Mustela erminea* (205 g; 55.7 g/d DFI)	0.12*	0.00017-0.00006	**706-2,000**
100% Weasel *Mustela nivalis* (63 g; 24.7 g/d DFI)	0.18*	0.00017-0.00006	**1,059-3,000**

* Based on a $PEC_{oral\ predator}$ of 0.46 mg a.s/kg rat bw, for a bait consumption of 100%.
** In the case of foxes in a short-term exposure situation the fraction of poisoned rodents in their diet might be below 1.

. The long-term secondary poisoning to mammals still remains. Only the application of proper risk reduction measures will fit for the purpose of abating this potential risk.

Secondary poisoning to birds. Tier 2. Long-term exposure.-

No reliable long-term toxicity studies on birds have been submitted, and therefore, the only possible comparisons are with the $PNEC_{birds}$ estimated from short-term studies, which is supported by additional information.

Tier 2 for secondary poisoning for non-target birds containing chlorophacinone obtained from areas in and around buildings. Long-term risk characterisation. Products P1 and P2.

Bait consumption	**$PEC_{oral\ bird}$** (mg a.s./kg food)	**$PNEC_{bird}$** (mg a.s./kg food)	**$PEC_{oral\ birds}$/ $PNEC_{birds}$**
Based on residues in the rat after 5 days of ingestion after last meal. No resistance situation			
100%	0.46	0.03	**15.3**
Based on residues in the rat after day 14 just after last meal. Resistance situation			
100%	0.23	0.03	**7.7**

The rapporteur suggests the additional estimation of the short-term risk, to estimate the risk associated to a single ingestion of rat carcasses, compared to a short-term PNEC derived from single dose toxicity data. The refinement has lowered the ratios several times but there is still a long-term risk of secondary poisoning to birds.

In a long-term situation, all mammals and birds are potentially at risk of primary poisoning and mammals more than birds. To minimise the likelihood of target rodents developing resistance to anticoagulant rodenticides, long-term deployment of bait blocks as a preventative control measure is not recommended. Product labels and approved guidance on good practice additionally instruct users to retrieve and securely dispose of all unconsumed baits at the end of control programmes. Both these factors limit the opportunity for exposure and reduce the primary poisoning risk to small non-target animals. Because of the toxic nature of rodenticides it is absolutely necessary to develop and validate risk management procedures in order to minimise the risk to non target animals.

As a conclusion it can be said that small mammals and birds are the most sensitive organisms; being mammals more prone to primary and secondary poisoning than birds. These risks estimations have been confirmed by two short-term dietary semi-field studies (*Pica pica* and ferrets, *Mustela putorius furo*) where there is a significant risk of secondary poisoning for mammals (55% mortalities) and a much lower risk to birds (no mortalities reported).

Open areas (Products P1 and P2)

Primary poisoning: The primary poisoning risks to birds and mammals from ingestion of bait blocks are assumed to be very low in open areas because delivery to the target animals is direct, the bait is not visible from above ground when the tunnel openings have been covered over and because the target rodents are unlikely to move pieces of bait block from protection underground to places where they may become accessible to non-target birds and mammals.

It is not possible to quantify the amount of bait block that may be exposed for ingestion by non-target birds and mammals. The levels of risk are considered to be very low, but in any event they are adequately covered by the assessments made above for various amounts of bait block directly ingested following use in and around buildings.

Secondary poisoning: The secondary poisoning risks to birds and mammals following the use of bait blocks containing chlorophacinone in open areas are adequately quantified for uses in and around buildings as above.

Waste dumps (Products P1 and P2)

Primary poisoning: It is not possible to estimate the amount of bait block that may be exposed for ingestion by non-target birds and mammals. Given that the attraction of waste dumps to the predominantly scavenging animals drawn there lies in the abundant availability of alternative food items, fragments of dyed bait blocks formulated to appeal specifically to target rodents would seem unlikely to make significant contributions to the daily food intake of individual non-target birds and mammals. The levels of risk are considered to be adequately represented by the assessments made above for various amounts of bait block directly ingested following use in and around buildings.

Secondary poisoning: The secondary poisoning risks to birds and mammals following the use of bait blocks containing chlorophacinone in waste dumps are adequately quantified for uses in and around buildings as above.

2.2.2.5.2. Risk characterisation Product P3 (tracking powder, 0.2%)

These use patterns have been employed for developing a tentative risk assessment. No exposure scenarios are currently available for this specific use. Thus, a case-specific approach is presented. The information is not sufficient for presenting a quantitative estimation, nevertheless, a qualitative assessment and some preliminary comparisons between toxicity and the expected exposure level are presented.

STP and aquatic compartment (including sediment) and groundwater

Inside buildings (Product P3)

Due to use patterns (holes and burrows within buildings) releases to water bodies are considered negligible.

Terrestrial compartment

Inside buildings (Product P3)

Due to use patterns (holes and burrows within buildings) releases to soil are considered negligible.

Non compartment specific effects relevant to food chain (primary and secondary poisoning) (Product P3)

Primary poisoning of domestic mammals within the treated buildings, and secondary poisoning of domestic mammals within the buildings and of wild birds and mammals surrounding the treated buildings are considered relevant and assessed below.

Inside buildings

Primary poisoning

Primary poisoning associated to the contact of non-target animals with the tracking power is very limited due to the use patterns. Contact with wild animals other than the pest is unlikely if the use pattern limitations are followed. Contact with domestic mammals, such as cats and dogs cannot be fully excluded.

The applicant suggests a typical application of 8 points with 25g of tracking powder per point; representing a total amount of 200 g of tracking powder per application. The powder contains 2000 mg chlorophacinone/kg product, and therefore, this amount represents eight points with 50 mg chlorophacinone/point, with a total of 400 mg chrorophacinone per application.

The acute toxicity of chlorophacinone to dogs is indicated through and LD_{50} expressed as much lower than 2 mg a.s/kg bw. The highest risk is expected for young puppies of cats and very low-size dog breeds (adult size equal to or lower than 5 kg). The expected size for a 30-day-old cat or dog, within these breeds, ranges from 0.25 to 1 kg. The risk can be tentatively presented as the amount of powder, and percentage of applied product, the animal should ingest for reaching the LD_{50}, and therefore for reaching a 50% likelihood of lethality. The calculations are presented below:

- A 50% risk of acute lethality is associated to the consumption by non target organisms (worst case) of less than 0.25-1 g of powder, representing less than 1-4% of the amount applied per point, and less than 0.125-0.5% of the total amount per application (8 points).

The exposure to these low amounts cannot be fully excluded even for professional applications, due to residues around the hole during the application or even associated to the movement of pest animals around the building. Thus, a potential acute risk associated to the use of the tracking powder formulation is identified and risk mitigation measures should be implemented.

The use patterns indicate that the application would continue for 21 days. Thus, a medium-term risk should be considered. The key study for this assessment is a 11 to 16 weeks subchronic oral toxicity test in rats. Mortality was the key effect and was recorded daily. The in-depth assessment of the study allows to estimate a short-term mortality LD_{50} ranging between 0.04 and 0.08 mg a.s/kg bw and day. This value is confirmed from the semifield study, in which an LD_{50} of about 0.064 mg a.s/kg bw and day, can be expected based on a 55% mortality at 0.32 mg a.s/kg bw distributed in five days. Using the 0.04 mg/kg bw and day value, the medium-term risk can be tentatively presented as the amount of powder, and percentage of applied product, the animal should ingest during several days for reaching this level, and, therefore, for reaching a 50% likelihood of lethality for repeated daily applications during a several days period. The calculations are presented below:

- A 50% risk of lethality is associated to the repeated consumption during several days (5-21) by non target organisms (worst case) of less than 0.005-0.02 g of powder, representing less than 0.02-0.08% of the amount applied per point, and less than 0.0025-0.01% of the total amount per application (8 points).

The exposure to these extremely low amounts cannot be fully excluded even for professional applications, due to residues around the hole during the application or even associated to the movement of pest animals around the building. Thus, a potential medium term risk associated to the use of the tracking powder formulation is identified and risk mitigation measures should be implemented.

The use patterns require taking out and handled appropriately the powder residues at the end of the treatment (21 days). The long-term toxicity endpoint is expressed by a NOEC of 0.005 mg a.s/kg bw

and day. Following a similar rationale as presented in the above calculations, residues leading to the potential exposure of non-target animals to 0.625-2.5 mg of product per day should be sufficient for reaching this NOEC value. These amounts are imperceptible even for trained professional applicators. Thus, a potential long term risk associated to the use of the tracking powder formulation is identified even if the powder is retired after the treatment period, and risk mitigation measures should be implemented.

Secondary poisoning

The use patterns are exclusively for indoor applications, however, as the efficacy depends on the exposure of pest animals to the rodenticide during several days, pest animals may be consumed by domestic mammals within the buildings as well as by wild birds and mammals around the buildings.

Secondary poisoning mostly depends on the accumulation of the rodenticide in the pest animal, being independent of the concentration of the rodenticide in the bait. The efficacy studies indicate an equivalent level of efficiency for the tracking powder and the wax baits, and therefore equivalent internal exposure doses (concentration in the pest animals which are ingested by the predators) are expected.

As a consequence, the risk associated to secondary poisoning is equivalent for the wax baits and the tracking powder, and the calculations presented for wax baits are also applicable to this formulation. Please see chapter 2.2.2.5.1. of this document.

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

Chlorophacinone is proposed for entry in Annex I of Directive 98/8/EC as an active substance for use as a rodenticide (product type 14) to control brown rat and house mouse. However, assessed from the documentation for the active substance, chlorophacinone, and the representative products: block bait, grain bait and tracking powder, it is concluded that the tracking powder formulation presents a human health risk from indirect exposure as a result of use. Moreover, a high risk for primary and secondary poisoning for birds and mammals has been identified for all of the representative products. The results confirm a risk for non-target mammals and a potential risk for birds. The assessment is based on results from a semi-field study, which also confirms the risk of secondary poisoning for mammals. Therefore, a further refinement of the risk assessment is not expected to modify this conclusion. Thus the authorization of this active substance will require risk mitigation measures for minimizing the exposure of non-target terrestrial vertebrates.

In the case of the tracking powder it has been recognised by the RMS and the TM that the risk mitigation measures agreed last March 2007 at the 24th CA meeting are not considered sufficient to prevent non-target mammals or birds from primary or secondary poisoning. Therefore further risk mitigations measures have been included in this section. Nevertheless, their efficacy is debatable and RMS proposal is to weigh up the need for a rodenticide in the form of tracking powder which is deployed in really very specific occasions where no other rodenticides are effective and the only possibility of fighting against the pest is the tracking powder.

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

It is recognised that anticoagulants like chlorophacinone do cause pain in rodents but it is considered that this is not in conflict with the requirements of Article 5.1 of the Directive “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.

As several anticoagulants have been assessed for possible Annex I entry at the same time, being quite similar regarding the hazardous properties and associated risks, the Commission initiated a work on possible risk mitigation measures for all anticoagulant rodenticides. A document describing possible risk mitigation measures for all anticoagulant rodenticides has been agreed at the 24th CA-meeting (CA-March07-Doc.6.3– final). The document distinguishes between measures to be taken into account at community level through restrictions in the Annex I entry decision, and measures that can be taken into account at national level when products are to be authorised. The proposal for Annex I decision in chapter 3.2 and the elements to be taken into account by Member States when authorising products, as described in Chapter 3.3, are based on this assessment report and on the Commission document on risk mitigation measures for anticoagulants used as rodenticides.

The standard risk reduction measures are not considered sufficient for covering the tracking powder application (Product 3). Therefore, the following specific risk mitigation measures should be employed to further reduce the risk to non-users and non-target organisms:

- Use by trained professionals only.
- Use this product only when the use of a traditional rodenticide bait is not suitable (e.g. where there are abundant natural foods that could reduce traditional bait take). Never use in areas where children, pets or other non-target vertebrates can have access. Mark the treated area and its surroundings with indications informing about the use of highly toxic tracking powder.
- Before use, wear gloves, suitable protective clothing and a dust filtering respirator.
- Do not apply where draughts are considered likely to disperse the powder.
- Take care to cover or to protect the areas of powder application with tiles, bait stations, piece of wood, etc., so that they are not accessible to, or consumed by non target animals.
- Do not use in areas where the powder could reach sewers, farm slurry, leachates, wastewaters, rainfall collectors, etc. due to normal practices, cleaning processes, or rainfall.
- If used in a non-industrial area (e.g. in farm buildings), where domestic animals may come into contact with dead rodents, the use of notices warning humans to keep domestic animals from treated areas should be considered.
- Dispose of dead rodents, bait stations, etc. as well as tiles, pieces of wood and the special devices used etc. which have also been in contact with the tracking powder according to local regulation. As the bodies may have powder on the fur, the use of gloves is recommended when collecting bodies (as rodents are known disease vectors, gloves should always be worn when handling dead rodents).
- Use of the most appropriate device for the tracking powder so that the spill is minimised as much as possible.
- Member States should consider the high risk of this application during national authorizations, and adopt the measures to guarantee that tracking powder is only used when no alternatives are feasible.

3.2. Decision regarding inclusion in Annex I

Chlorophacinone shall be included in Annex I of Council Directive 98/8/EC as an active substance in rodenticides (product type 14), subject to the following specific provisions according to Article 10(2)(i)(a-f) of Directive 98/8/EC. The active substance, chlorophacinone, as manufactured, should have a minimum purity of 978 g/kg.

In view of the identified risks for non-target animals, the active substance shall 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 products other than tracking powder shall not exceed 50 mg/kg and only ready-for use products shall be authorised.

(2) Products to be used as tracking powder shall only be placed on the market for use by trained professionals.

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

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

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

- The results on human health risk assessment of the representative products for blocks and grain baits concluded that these can be used by professional and non professional users. However, the representative product, tracking powder, due to the risk identified in the indirect exposure as result of use, only will be placed in the market for use by professionals trained and appropriate risk mitigation measures must be taken at product authorisation level. Namely, the ones listed in section 3.1.

- Biocidal product containing chlorophacinone must be authorized in a way that ensures the use of the products to be protected such as the exposure to humans and animals, primary as well as secondary exposure, is minimized as much as possible.

- Tracking powder showed an unacceptable risk for non-users. Therefore, this product should only be used by trained professionals in places with restricted access to prevent secondary exposure of bystanders, particularly infants and children, as well as non-target animals. Member States should consider the high risk of this application during national authorizations, and adopt the measures to guarantee that tracking powder is only used when no alternatives are feasible.

- Chlorophacinone baits should not be placed such that food, feeding stuffs or drinking water could be contaminated.

- 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.

- 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.

- 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 minimise the risk of consumption by non-target animals or children. Where possible, secure baits so that they cannot be dragged away.

    - Search 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 persons, do not use anticoagulant rodenticides as permanent baits

    - Remove all baits after treatment and dispose them of 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 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.)

- Adequate safety instructions (including use of appropriate personal protective equipment, PPE) should be provided in the use instructions.

- 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 chlorophacinone 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.

The abovementioned measures should constitute the foundation for the authorisation process of biocidal products at Member State level.

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

3.5. Updating this Assessment Report

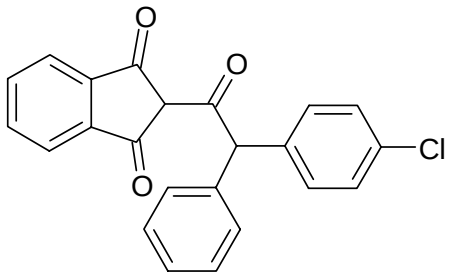
This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information referred to in Articles 7, 10.4 and 14 of Directive 98/8/EC. Such adaptations will be examined and finalised in connection with any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

Appendix I: List of endpoints

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

Active substance (ISO Common Name)	Chlorophacinone
Product-type	Main group 03: Pest control Product type 14: rodenticides, against rats and mice

Identity

Chemical name (IUPAC)	2-[2-(4-chlorophenyl)-2-phenylacetyl]indan-1,3-dione
Chemical name (CA)	-
CAS No	3691-35-8
EC No	223-003-0
Other substance No.	CIPAC No. 208
Minimum purity of the active substance as manufactured (g/kg or g/l)	978 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None
Molecular formula	C23H15ClO3
Molecular mass	374.82
Structural formula	

Physical and chemical properties

Melting point (state purity)	143.0°C (99.74%)
Boiling point (state purity)	Decomposed below boiling point
Temperature of decomposition	250 ºC
Appearance (state purity)	Pale yellow powder (99.85%)
Relative density (state purity)	1.4301g/mL (99.85%)
Surface tension	68.9 mN/m (20.6 ºC)
Vapour pressure (in Pa, state temperature)	4.76 x 10^{-4} Pa at 23°C
Henry's law constant (Pa m^3 mol^{-1})	0.013725 Pa.m^3.mol^{-1} Log H: -1.86
Solubility in water (g/l or mg/l, state temperature)	pH4: 1 mg/L at 20°C
	pH7: 344 mg/L at 20°C
	pH10: 476 mg/L at 20°C
Solubility in organic solvents (in g/l or mg/l, state temperature)	Pure water: 13 mg/L at 20°C
	Hexane: 854 mg/L at 25°C
Stability in organic solvents used in biocidal products including relevant breakdown products	Active substance is not formulated in solvents in biocidal products
Partition coefficient (log P_{OW}) (state temperature)	pH4: 3.08 at 23°C
	pH7: 2.42 at 23°C
	pH10: 2.57 at 23°C
	No pH control: 1.93 at 23°C
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH_4_: > 1 year at environmentally relevant temperatures.
	pH_7_: > 1 year at environmentally relevant temperatures.
	pH_9_: > 1 year at environmentally relevant temperatures.
Dissociation constant	pKa = 8.0
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Approximately 260nm and 315nm - ε not stated
Photostability (DT_{50}) (aqueous, sunlight, state pH)	Under artificial sunlight: DT_{50} 2.2 days (natural summer sunlight at latitude 50°N) in buffer solution (pH 7).

	DT_{50} 1.3 days (natural summer sunlight at latitude 50°N) in pond water (pH 8.4 post sterilisation).
Quantum yield of direct phototransformation in water at Σ > 290 nm	Not determined.
Flammability	Not highly flammable
Explosive properties	Not explosive

Classification and proposed labelling

with regard to physical/chemical data	None.
with regard to toxicological data	T+ **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.
Specific concentration limits	C≥0.7% T^+; R61- 26/27/28-48/23/24/25 0.5%≤C<0.7% T^+; R61-26/27-25-48/23/24/25 0.1%≤C<0.5% T^+; R26/27-25-48/23/24/25 0.07%≤C<0.1% T^+; R26/27-22-48/20/21/22 0.01%≤C<0.07% T; R23/24-22-48/20/21/22 0.001%≤C<0.01% Xn; R20/21
with regard to fate and behaviour data	None.
with regard to ecotoxicological data	N **R50/53** Very toxic to aquatic organisms may cause long-term adverse effects in the aquatic environment

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	The technical material is dissolved in the mobile phase (0.1 g ammonium acetate + 42 mL 0.05 N hydroxide tetrabutylammonium solution in phosphate buffer + 14 mL THF + 44 mL methanol). Determination is by reverse-phase HPLC/UV with a Spherisorb ODS 2 column with mobile phase as described above (230 nm).
Impurities in technical active substance (principle of method)	See Confidential Information document.

Analytical methods for residues

Soil (principle of method and LOQ)	Soil is extracted by shaking with aqueous methanol. Determination of the filtered and diluted extract is by reverse-phase LC-MS/MS (monitored ions 373.4/201.2 m/z). A Luna C-8 column is used with acetonitrile/water/ammonium acetate (gradient) mobile phase. The limit of determination is 0.01 mg/kg (defined as the lowest concentration at which acceptable recovery has been demonstrated).

Air (principle of method and LOQ)	Air is passed through Tenax absorption tubes which are eluted with acetonitrile. Determination is by reverse-phase HPLC, Luna C-8 column with acetonitrile/water/ ammonium acetate (gradient) mobile phase. The limit of determination is 0.03 μg/m^3 (defined as the lowest concentration at which acceptable recovery has been demonstrated).
Water (principle of method and LOQ)	Water is extracted by partition into dichloromethane. The extract is evaporated to dryness and reconstituted in aqueous methanol. Determination is by reverse-phase LC-MS/MS (monitored ions 373.4/201.2 m/z). A Luna C-8 column is used with acetonitrile/water/ ammonium acetate (gradient) mobile phase. The limit of determination is 0.05 μg/L (defined as the lowest concentration at which acceptable recovery has been demonstrated).
Body fluids and tissues (principle of method and LOQ)	Blood Blood is diluted with methanol. Phosphate buffer, a mixture of ethanol/ethyl acetate and trichloroacetic acid solution is added. The sample is shaken and the organic phase removed. The sample is re-extracted with ethanol/ethyl acetate. The combined organic extracts are evaporated to dryness and reconstituted in methanol prior to determination. Determination is by HPLC with a Thermo Hypersil Keystone column and ammonium acetate/methanol (gradient) mobile phase (two ion transitions monitored 373>201 and 375>203). The limit of determination is 0.05 mg/L (defined as the lowest concentration at which acceptable recovery has been demonstrated). Liver Liver is blended with phosphate buffer (pH 5.5) and a mixture of ethanol and ethyl acetate (1+19, v/v). A solution of trichloroacetic acid is added and the sample is blended again. Clean-up of the centrifuged extract is by GPC. Determination is by HPLC with Thermo hypersil keystone column and ammonium acetate/methanol (gradient) mobile phase (two ion transitions monitored 373>201 and 375>203). The limit of determination is 0.05 mg/L (defined as the lowest concentration at which acceptable recovery has been demonstrated).
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Samples are extracted by blending twice with methanol (meat and lemon) or methanol/water (oil-seed rape). After centrifugation the samples are diluted with methanol/water. Determination is by HPLC/MS-MS LOQ: 0.01 mg/kg

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Compound is absorbed, enters the enterohepatic circulation and then is excreted through the faeces. Metabolism studies in rats with radiolabelled Chlorophacinone showed that it is absorbed following oral administration, with a relatively short (10.2 hours) plasma half-life. After a single low dose (1-1.4 mg/Kg), 90% radioactivity is excreted in faeces within 48 hours and 100% of the administered material is excreted within 4 days. Higher doses (2 mg/kg) showed that at 168 hours excretion is incomplete and 8% of dose was still present in the carcass. Elimination was mainly via faeces, with less than 1% of urinary excretion, and no excretion via expired air. About 19.6% of the faecal radioactivity (equivalent to 15% of dosed radioactivity) is unchanged parent compound and most were metabolised compounds. Two main metabolites was identified as hydroxylated metabolites accounting for the 45% of faecal radioactivity (36.2% of administered dose) with some "minor" unidentified metabolites representing 34% of faecal radioactivity. It is important to note that a peak representing 12.49 % of assigned peaks (representing about 8 % of dosed radioactivity) was detected but not identified.
Rate and extent of dermal absorption:	• The in vitro topical application of ^{14}C-Chlorophacinone as a tracking powder formulation or wheat flour bait to human split thickness skin samples maintained ***in vitro*** resulted in similar **rapid rates of absorption** with radioactivity appearing within 1.7 or 0.25 hours respectively **but absorption was minimal** and less than 0.1% (powder) or 0.5 % (bait) were detected in the receptor fluid. • **Total absorption in human skin is estimated to be not more than 1.7%., deduced in vitro test using** topical application of ^{14}C-Chlorophacinone as a tracking powder formulation or wheat flour bait to human split thickness skin samples maintained *in vitro*, considering total absorption including radioactivity measured in receptor fluid, tape stripping and residual skin values.
Distribution:	Compound is absorbed, enters the enterohepatic circulation and then is excreted through the faeces. Maximum blood concentration is reached after 4 hr. In a single dose oral study in the rat the tissue

	distribution was calculated 48 hours after dosing for several tissues: Liver (2.9 ppm), kidney (1.18 ppm), lung (0.39 ppm, heart (0.16 ppm), muscle (0.097 ppm), fat (0.673 ppm), carcass (0.306 ppm). The levels in the liver were five times higher than those in the kidney four hours after dosing and 2.8 fold at the 48 hour post-dosing sacrifice point.
Potential for accumulation:	The blood half-life for elimination is 10 hr. In a study dosing 1-1-4 mg/kg, the results indicate rapid absorption and relatively rapid metabolism in the liver and 100% elimination within four days. However, higher doses (2 mg/kg) showed that at 168 hours **excretion is incomplete** with **8%** of dose was still present in the carcass.
Rate and extent of excretion:	Elimination was mainly **via faeces**, with less than 1% urinary and CO2 excretion: Faecal excretion 101.6% after 4 days (Biliary excretion after 8 hr is 26%) Urinary excretion 0.75% after 4 days Most faecal excretion was as metabolised compounds accompanied with **unchanged parent compound (19.6%** of the faecal radioactivity, equivalent to 15% of dosed radioactivity). Two major **metabolites represented for 45%** of faecal radioactivity (equivalent to 36.2 % of total dosed radioactivity) as hydroxylated metabolites, with some "minor" unidentified metabolites.
Toxicologically significant metabolite(s)	Two main metabolites were identified as hydroxylated metabolites, one in the indandione group and the other in the biphenyl portion of the molecule. The two analogues constituted 46% of faecal radioactivity (36.2% of administered dose). A metabolite presented as 12% of faecal radioactivity (8% of extracted material) was not identified as well as other minor metabolites representing 34% of faecal radioactivity. After 168 hours excretion was incomplete and about 8% was detected in carcases. Applicant argues that "none of the metabolites identified for indandione derivatives used as rodenticides have been shown to be toxicologically significant". However no data is presented to justify this statement.

Acute toxicity

Rat LD_{50} oral	**Male: 3.15 mg/kg** (1.48 - 6.68) Female: 10.95 mg/kg (6.46 - 18.57) Combined: 6.26 mg/kg (3.96 - 9.89) Mortalities in males (4/10) observed from the lowest dose (2 mg/kg bw)
Rat LD_{50} dermal	LD_{50} (male and female) <<2mg/kg bw (all males died at all doses) Males **0.329 mg/kg bw**
Rat LC_{50} inhalation	Male: 7.0 µg/L (0.83-59.0) Female: 12.0 µg/L (7.80-18.0) Combined: 9.3 µg/L (2.30-38.0)
Skin irritation	Average erythema score over 24, 48, 72 h = 0.00 for non-abraded skin Average oedema score over 24, 48, 72 h = 0.00 for non-abraded skin. Chlorophacinone does not meet EU criteria for classification as a skin irritant
Eye irritation	Average score over 24, 48, 72 h for : corneal reaction = 0.00 iridial reaction = 0.00 conjunctival redness = 0.00 conjunctival swelling = 0.00 Chlorophacinone does not meet EU criteria for classification as an eye irritant
Skin sensitization (test method used and result)	No signs of irritation were observed. Chlorophacinone does not meet EU criteria for classification as a skin sensitization

Repeated dose toxicity

Species/ target / critical effect	Rat (90 day oral administration) No target organs were identified. The mode of action for anticoagulant rodenticides is well characterised. The critical effect is death arising from persistent or severe haemorrhage. The clinical findings in the study were indicative of internal haemorrhagic events and were consistent with the established pattern of increasing prothrombin times associated with increasing severity of bleeding from orifices or abrasions, pallor, ataxia or weakness/limb paralysis and breathing difficulty. Death followed development of signs and necropsy confirmed presence of haemothorax and haemoperitoneum among other diffuse, non-specific haemorrhages and haematoma formation. Rabbit (15 day dermal administration, 5 days/week

	for 3 weeks) Widespread non-specific haemorrhage was the primary cause of death among rabbits dosed with a 2% formulation of chlorophacinone. Necropsy also revealed centrilobular liver necrosis. In-life signs of haemorrhage were confirmed by necropsy observations of free fluid in many body cavities and pale organs. Increased prothrombin times were measured in-life as an indicator of progressive failure of the clotting cascade arising from non-replenishment of Vitamin K in the liver of intoxicated animals.
Lowest relevant oral NOAEL / LOAEL	Rat: LOAEL = 0.010 mg/kg b.w. /day established on the basis of 16 weeks dosing period with minimal increase but statistically significant in coagulation time and other biochemical parameters alteration which are suggestive of hepatic and renal disorders NOAEL = 0.005 mg/kg b.w. /day (11 weeks exposure) (Some uncertainty due to shorter time at the dose of 5 µg/kg b.w. /day and no prothrombine time determination at this dose)
Lowest relevant dermal NOAEL / LOAEL	Rabbit: LOAEL 0.40 mg/kg/day observation the alteration of prothrombin times NOAEL 0.08 mg/kg/day (21 day exposure)
Lowest relevant inhalation NOAEL / LOAEL	Not established - study not scientifically justified

Genotoxicity	Results for *in vitro* bacterial gene mutation; *in vitro* cytogenicity in mammalian cells and *in vitro* mammalian cell gene mutation tests were negative. The mouse micronucleus test was also negative.

Carcinogenicity

Species/type of tumour	The closely related molecule warfarin is not carcinogenic to humans. Study on chlorophacinone is not available. Applicant argument for non submission of data was accepted.
lowest dose with tumours	Not appropriate

Reproductive toxicity

Species/ Reproduction target / critical effect	The closely related molecule warfarin shows no adverse effects on human fertility. Study on

	chlorophacinone is not available. Applicant argument for non submission of data was accepted.
Lowest relevant reproductive NOAEL / LOAEL	Not appropriate
Species/Developmental target / critical effect	Rat There were no developmental targets identified. No adverse effects any gestational parameters, including pre- or post-implantation loss, number of foetuses per litter, foetal sex ratio, or foetal body weight per litter were observed. There was no adverse effect on the foetus - no developmental toxicity or teratogenicity evident (external, visceral, skeletal, or total malformations or variations) even at the high dose that resulted in marked maternal fatality (72% in the high dose group). The critical effect was maternal death following haemorrhagic events during pregnancy (72% at the highest dose of100 µg/kg bw). Rabbit There were no developmental targets identified in the pregnant rabbit. High maternal mortality 81% and 100% in the two highest dose groups (25 and 75 µg/kg bw) was accompanied by signs typical of an anticoagulant rodenticide (external bleeding, pale extremities, pale organs, blood in gastrointestinal tract and amniotic sacs of the uterus. Chlorophacinone administered to pregnant rabbits for 13 consecutive days during gestation at dose levels of 0, 5.0, 10.0, 25.0, 75.0 µg/kg/day did not affect female fertility, gestational parameters nor cause embryotoxic effects. There was no evidence of treatment related changes in incidence of individual or pooled external, visceral, skeletal or total malformations or variations. Morphological examinations revealed no teratogenic potential. It is a matter of discussion if the standard teratogenicity test is appropriate for anticoagulant rodenticides, in particular when data is intended to be used to deduce no classification for reproduction-development as the embryogenesis period is not tested and no study of two generation reproduction may be tested. Classification of all anticoagulant rodenticides from read across from warfarin has been suggested on the basic of the teratogenic/embryotoxicity properties of warfarin and concluded in Expert Committee meeting. This would mainly affect to decision for CL but probably not for quantitative values of NOAEL to

	be used for risk assessment.
Developmental toxicity	
Lowest relevant developmental NOAEL / LOAEL	Rat maternal LOAEL – 100 µg/kg/day. Rat maternal NOAEL – 50.0 µg/kg/day. Embryofoetal toxicity – LOAEL - >100.0 µg/kg/day Rabbit maternal LOAEL – 25.0 µg/kg/day Rabbit maternal NOAEL – 10.0 µg/kg/day Embryofoetal toxicity – LOAEL - >25.0 µg/kg/day

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	Difethialone, a closely related molecule, showed no antianginal activity *in vivo* or *in vitro;* no antihypertensive activity; no sedative activity; no anticonvulsant activity; no antidepressant activity; no antispasmodic activity in a variety of *in vitro* tests and no analgesic, anti-inflammatory or gastric antiacid activity in various tests designed to investigate these pharmacological endpoints. Chlorophacinone, like difethialone, has a highly specific mode of action, blocking regeneration of Vitamin K in the liver and no other pharmacologic activity has been established for the molecule.
Lowest relevant developmental NOAEL / LOAEL.	Not established

Other toxicological studies

	One study in male rats investigated the efficacy of antidotal treatment. The animals were provided chlorophacinone pellets (5ppm) as a diet replacement for 1, 2 or 3 days. Vitamin K_1 antidote was injected intravenously to half of the animals in each group, 1-2 hours after completion of exposure period and followed by oral administration of phytomenadione for up to 13 days. Prothrombin times were monitored to detect increases during treatment and decreases following antidotal treatment. All animals given 1, 2 or 3 meals with chlorophacinone died. Antidotal treatment was successful following 24 hour exposure but less successful with longer periods of exposure. The study demonstrated the effectiveness of Vitamin K_1 (phytomenadione) as an antidote to anticoagulant intoxication in the rodent **if the exposure is limited to around the LD_{50}, but not if the dose is**

	excessive.

Medical data

	There are no published data on specific cases of Chlorophacinone intoxication, and no case reports from the manufacturer concerning adverse effects in users applying the products. Anticoagulant rodenticides such as Chlorophacinone function by inhibiting the ability of the blood to clot at the site of a haemorrhage, by blocking the regeneration of vitamin K in the liver. Information relating to medical supervision of staff involved in research and development, production and packaging of second generation rodenticides is included; a description of the well researched mode of action and specific medical effects arising from accidental or intentional exposure of humans to anti Vitamin K rodenticides. The closely-related active substance warfarin has been in use for over forty years as an anticoagulant drug in human medicine. Its use is described in more detail in 3, but in summary it has been used in millions of patients with clotting disorders, heart disease, atrial valve replacement, and more recently, deep vein thrombosis. Use is life-long for most patients with heart disease, clotting disorders or valve replacement. There have been no reports of any increase in tumour incidence or of any adverse effects on human fertility. There have been no reports of neurotoxic or neurodegenerative disease, or neuro-muscular disease associated with the use of warfarin. The specific medical effect can be recognized by simple tests such as clotting time, Quick test or prothrombin rate determinations and the antidotal treatment regimen is well characterized – parenteral injection of Vitamin K_1 (phytomenadione) followed by long term oral administration of the antidote to stabilize prothrombin times. This regimen has been effectively and successfully used within the manufacturing plants and no cases of intoxication have been reported between 1987 and 1999 (last available information).

Summary	Value	Study	Safety factor
Non-professional user			
ADI (acceptable daily intake, external long-term reference dose)	Not applicable		
AOEL-S (Operator Exposure)	0.000017 mg/kg bw/day (repeated dose). No acceptable acute dose study for risk characterization 0.000033 mg/kg bw/day (acute exposure)	90 day rat oral toxicity A 6.4.1-01 NOAEL = 0.005 mg/kg bw/day Maternal toxicity in teratogenicity study in rabbit (NOAEL= 0.010 mg/kg bw/day)	300
ARfD (acute reference dose)	Not applicable		

Acceptable exposure scenarios (including method of calculation)

Professional users

PRODUCT P1 (wax blocks baits, used as supplied) are used in sewers, areas in and around buildings, open areas and waste dumps. Products are supplied loose and in protective LDPE sachets for use by professional users, to prevent dermal and inhalation exposure of users. To represent the worst-case, assessments are made for product not in sachets. Where appropriate, exposure assessments are based on default values in EU Guidance Document Section 7.2 of Part 3 June 2002. In addition, exposure assessments are also done using values derived from two operator exposure studies.

Professional user: assessment based on default values

Workplace operation	PPE	Total systemic dose (mg/kg bw/day)	MOE
Treating 75 cesspools/day in sewers to control rats; unused product not collected.	Gloves	0.0000201	249
	None	0.0001992	25
Treating 75 bait points/ day to control rats in/around buildings and waste dump (landfill) perimeters; unused product collected	Gloves	0.00001215	412
	None	0.0001197	42
Treating 75 bait points/ day to control mice in/around buildings and waste dump (landfill) perimeters; unused product collected	Gloves	0.00000816	613
	None	0.0000798	63
Treating 75 bait points/ day (burrows) in open areas to control rats and mice; unused product not collected	Gloves	0.00000618	809
	None	0.00006	83

Professional users

Professional user: assessment based on measured values

Treating 75 cesspools/day in sewers to control rats; unused product not collected.	Gloves	0.0000019125	2614
	None	0.000019125	261
Treating 75 bait points/ day to control rats in/around buildings and waste dump (landfill) perimeters; unused product collected	Gloves	0.00000201	2488
	None	0.0000201	249
Treating 75 bait points/ day to control mice in/around buildings and waste dump (landfill) perimeters; unused product collected	Gloves	0.00000201	2488
	None	0.0000201	249
Treating 75 bait points/ day (burrows) in open areas to control rats and mice; unused product not collected	Gloves	0.0000019125	2614
	None	0.000019125	261

Professional users	PRODUCT P2 (grains baits, used as supplied) is used in and around buildings, open

areas and waste dumps. Grain products containing chlorophacinone are not used in sewers. Products are supplied loose and in protective LDPE sachets for use by professional users, to prevent dermal and inhalation exposure of users. To represent the worst-case, assessments are made for product not in sachets. Where appropriate, exposure assessments are based on default values in EU Guidance Document Section 7.2 of Part 3 June 2002. In addition, exposure assessments are also done using values derived from two operator exposure studies.

Professional user: assessment based on default values

Workplace operation	PPE	Total systemic dose (mg/kg bw/day)	MOE
Treating 80 bait points/day to control rats in/around buildings and waste dump (landfill) perimeters; unused product collected	Gloves	0.000000625	8000
	None	0.00000445	1124
Treating 80 bait points/day to control mice in/around buildings and waste dump (landfill) perimeters; unused product collected	Gloves	0.000000625	8000
	None	0.00000445	1124
Treating 80 bait points/ day (burrows) in open areas to control rats and mice; unused product not collected	Gloves	0.000000625	8000
	None	0.00000445	1124

Professional user: assessment based on measured values

Treating 80 bait points/day to control rats in/around buildings and waste dump (landfill) perimeters; unused product collected	Gloves	0.00000064	7813
	None	0.00000352	1420
Treating 80 bait points/day to control mice in/around buildings and waste dump (landfill) perimeters; unused product collected	Gloves	0.000000415	12048
	None	0.00000217	2304
Treating 80 bait points/ day (burrows) in open areas to control rats and mice; unused product not	Gloves	0.00000065	7692
	None	0.0000036	1389

	collected			
	PRODUCT P3. PRODUCT P3 is used inside buildings and also used in rodent burrows, mouse holes where other baits cannot be easily placed. The product is only applied by professional users. Professional users (e.g. from private companies and local authorities) are trained operators who handle all product types on a daily basis. They can be expected to wear protective clothing (gloves) when handling PRODUCT P3. After use, unused product is unlikely to be collected because it is placed in inaccessible areas. Where appropriate, exposure assessments are based on default values in EU Guidance documents, although there is no suitable model for a rodenticide tracking powder. Therefore, default values from two other models are used, namely the BBA model for handling wettable powder pesticide formulations prior to applying a spray by hand-held equipment and the HSL model for surface spraying These default values can be related to the various tasks when handling.			
	Workplace operation	**PPE**	**Total systemic dose (mg/kg bw/day)**	**MOE [a]**
	Professional user: assessment based on default values (HSL model)			
	Treating 17 points/day; unused product not collected.	Gloves	0.000011	454
		None	0.0000722	70
	Professional user: assessment based on default values (BBA model)			
	Treating 17 points/day; unused product not collected.	Gloves	0.0000021	2380
		None	0.0000125	387

Non-professional users				
	Non-professional user: assessment based on default values			
	Treating 5 bait points/day to control rats; unused product collected	None	0.00000816	1815
	Treating 5 bait points/day to control mice; unused product collected	None	0.00000551	1815
	Non-professional user: assessment based on measured values			
	Treating 5 bait points/day to control rats; unused product collected	None	0.00000178	5618
	Treating 5 bait points/day to control mice; unused product collected	None	0.00000178	5618

	PRODUCT P2			
	Workplace operation	**PPE**	**Total systemic dose (mg/kg bw/day)**	**MOE**
	Non-professional user: assessment based on default values			
	Treating 5 bait points/day to control rats; unused product collected	None	0.000000465	21505
	Treating 5 bait points/day to control mice; unused product collected	None	0.000000465	21505

Indirect exposure as a result of use	PRODUCT P1 AND PRODUCT P2			
	Workplace operation	**Exposure path**	**Total systemic dose (mg/kg bw/day)**	**MOE**
	In sewers, waste dump perimeters and open areas for control of rats and mice.	None (Non-users will not be present during or after application)	–	–
	In and around buildings for control of rats and mice.	Non-users will not be present during application. Infants may ingest part of wax blocks.	0.00005	200
	PRODUCT P3			
	Workplace operation	**Exposure path**	**Total systemic dose (mg/kg bw/day**	**MOE**
	Inside buildings to control rats and mice.	Non-users will not be present during application. Adults or children may handle dead rodents without gloves	0.00057 (adults)	17
			0.0023 (children)	4

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)	pH~4_____: > 1 year at environmentally relevant temperatures (50ºC pre-test; 60, 70ºC).
	pH~7_____: > 1 year at environmentally relevant temperatures (50ºC pre-test).
	pH~9_____: > 1 year at environmentally relevant temperatures (50ºC pretest).
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Under artificial sunlight (25ºC): DT_{50} 2.2 days (natural summer sunlight at latitude 50°N) in buffer solution (pH~7). DT_{50} 1.3 days (natural summer sunlight at latitude 50°N) in pond water (pH~8.4 post sterilisation).
Readily biodegradable (yes/no)	No.
Biodegradation in seawater	Not applicable (exposure to seawater unlikely).
Non-extractable residues	Not applicable (exposure to aquatic systems unlikely).
Distribution in water / sediment systems (active substance)	Not applicable (exposure to aquatic systems unlikely).
Distribution in water / sediment systems (metabolites)	Not applicable (exposure to aquatic systems unlikely).

Route and rate of degradation in soil

Mineralization (aerobic)	61% AR after $_{ca}$ 100 days.
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20°C, aerobic): At 25°C DT_{50} value 47.3 days (1 soil, 75% 1/3 bar moisture).
	DT_{90lab} (20°C, aerobic): At 25°C DT_{90} value > 200 days (1 soil, 75% 1/3 bar moisture).
	DT_{50lab} (10°C, aerobic): estimated at 12°C from data available at 25°C. DT_{50} value 128 days (1 soil).
	DT_{50lab} (20°C, anaerobic): Not applicable.
Non-extractable residues	11.0% AR after 182 days.
	Degradation in the saturated zone: Not applicable.
Field studies (state location, range or median with number of measurements)	DT_{50f}: Not applicable.

	DT_{90f}: Not applicable.
Anaerobic degradation	Not applicable.
Soil photolysis	DT_{50} =11.1 d (12ºC) Degradation of chlorophacinone results in the formation of a major metabolite o-phthalic acid (37.1% AR), carbon dioxide (potentially 50% AR) and three minor degradation products (< 10% AR)
Non-extractable residues	9.0% AR after *ca* 100 days.
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	No significant metabolites were formed.
Soil accumulation and plateau concentration	Not applicable (not applied directly to soil).

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	Soil distribution (partition) coefficient (K_D) = 36 to 492 ml/g. Freundlich soil adsorption coefficient (K_F) = 80 to 1000 ml/g. Freundlich soil adsorption coefficient normalised for organic carbon content (K_{oc}) = 15,600 to 136,000 ml/g.

Fate and behaviour in air

Direct photolysis in air	The photochemical oxidative degradation half-life of chlorophacinone in air was estimated using the Atmospheric Oxidation Program v1.90 (AOPWIN), which is based on the structural activity relationship (QSARs) methods developed by Atkinson, R (1985 to 1996). The half-life for the hydroxyl reaction in air is estimated to be 14.3 hours, indicating that if present in air, chlorophacinone would not be expected to persist.
Quantum yield of direct photolysis	Not determined.
Photo-oxidative degradation in air	Latitude: ....n.a... Season: ... ..n.a... DT_{50} .. ..n.a....
Volatilization	Vapour pressure at 22.8°C is $4.76 \cdot 10^{-4}$ Pa (OECD 104). Henry's law constant = 0.013725 $Pa.m^3.mol^{-1}$ (based on a water solubility of 13.0 mg/l). Chlorophacinone is therefore not considered volatile and is not expected to volatilise to air in significant quantities.

Monitoring data, if available

Soil (indicate location and type of study)	No monitoring data available.
Surface water (indicate location and type of study)	No monitoring data available.
Ground water (indicate location and type of study)	No monitoring data available.
Air (indicate location and type of study)	No monitoring data available.

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	96 hours	Mortality	LC_{50} = 0.45 mg a.s/l
Invertebrates			
Daphnia magna	48 hours	Immobility	EC_{50} = 0.64 mg a.s/l
Algae			
Desmodesmus subspicatus (formerly known as *Scenedesmus subspicatus*)	72 hours	Biomass Biomass Growth rate Growth rate	E_bC_{50} = 1.7 mg a.s/l $NOEC_b$ = 0.72 mg a.s/l E_rC_{50} = 2.2 mg a.s/l $NOEC_r$ = 0.72 mg a.s/l
Microorganisms			
Activated sludge	3 hours	Respiration inhibition	EC_{50} > 1,000 mg a.s/l; above the water solubility limit EC_{15} > 775 mg a.s/l; above the water solubility limit

Effects on earthworms or other soil non-target organisms

Acute toxicity to *Eisenia foetida*	14-day LC_{50} > 300 mg a.s/kg wwt soil (synthetic OECD substrate).
Reproductive toxicity to ……	Not appropriate.

Effects on soil micro-organisms

Nitrogen mineralization	Waived.
Carbon mineralization	Waived.

Effects on terrestrial vertebrates

Acute toxicity to mammals	LD_{50} = 1.48 to 18.57 mg a.s/kg bw (rats)
Acute toxicity to birds	5-daysLD_{50} = 257 mg a.s/kg bw (Bobwhite quail)
Dietary toxicity to birds	5-days LC_{50} = 95 mg a.s/kg food (Bobwhite quail)

Reproductive toxicity to birds	Lowest 90-days NOEC (mortality) = 1 mg a.s/kg food (Japanese quail)

Effects on honeybees

Acute oral toxicity	Not appropriate.
Acute contact toxicity	Not appropriate.

Effects on other beneficial arthropods

Acute oral toxicity	Not appropriate.
Acute contact toxicity	Not appropriate.
Acute toxicity to ……..	Not appropriate

Bioconcentration

Bioconcentration factor (BCF) aquatic	Waived. No study available. The BCF_{fish} was calculated from the log K_{ow} of 2.42; pH~7, 23ºC according to the TGD and resulted in BCF_{fish} of 22.75 l/kg.
Depration time (DT_{50}) (DT_{90})	Waived.
Level of metabolites (%) in organisms accounting for > 10 % of residues	Waived.

Chapter 6: Other End Points

Appendix II: List of Intended Uses

PRODUCT P1 is used in the following areas:

- Sewer systems: professional use only
- In and around buildings: professional and non-professional use
- Waste dump (landfill) perimeters: professional use only. [Use in waste dumps (landfills) is restricted to perimeters only; the central areas are not treated.]
- Open areas: professional use only

PRODUCT P2 is used in the following areas:

- In and around buildings: professional and non-professional use
- Waste dump (landfill) perimeters: professional use only. [Use in waste dumps (landfills) is restricted to perimeters only; the central areas are not treated]
- Open areas: professional use only

PRODUCT P3 is only applied by professional users:

- Inside buildings. The product is not used routinely, but in emergency situations in limited quantities where rodent populations are very high and where competition for food makes control with baits impractical or inappropriate.
- In rodent burrows, mouse holes where other baits cannot be easily placed.

Appendix III: List of studies

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

Active substance

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
Section 1			No study reports submitted		
Section 2 A2.7/01	Schmit, T	2003	Analysis of Rozol rodenticide technical powder, EPA Reg. No. 7173-75. Liphatech, Inc., laboratory report no. 03093. GLP/Unpublished. *This report contains confidential information.*	Y	Lipha
Section 2 A2.8.9/01	Schmit, T	2003	Analysis of Rozol rodenticide technical powder, EPA Reg. No. 7173-75. Liphatech, Inc., laboratory report no. 03093. GLP/Unpublished. *This report contains confidential information.*	Y	Lipha
Section 3 A3.1.1/01	Hoffman, M.	1988 a	Melting point/melting range determination of chlorophacinone. Hazleton Laboratories America, Inc., laboratory report no. HLA 6001-221. GLP/Unpublished.	Y	Lipha
Section 3 A3.1.1/02	Kramer, H., Marion, T	2002 a	Melting point, bulk density, pH and accelerated stability of chlorophacinone. Covance Laboratories Inc., laboratory report no. 6372-110. GLP/Unpublished.	Y	Lipha
Section 3 A3.1.2/01	Tognucci, A.	2002	Determination of the boiling point/boiling range of chlorophacinone. RCC, laboratory report no. 844813. GLP/Unpublished.	Y	Lipha

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
Section 3 A3.1.3/01	Pesselman, R.	1990	Density determination of chlorophacinone (CPN). Hazleton Laboratories America, Inc., laboratory report no. HLA 6001-602. GLP/Unpublished.	Y	Lipha
Section 3 A3.1.3/02	Kramer, H., Marion, T	2002 a	Melting point, bulk density, pH and accelerated stability of chlorophacinone. Covance Laboratories Inc., laboratory report no. 6372-110. GLP/Unpublished.	Y	Lipha
Section 3 A3.2/01	Hoffman, M.	1988 b	Vapor pressure determination of chlorophacinone (CPN). Hazleton Laboratories America, Inc., laboratory report no. HLA 6001-217. GLP/Unpublished.	Y	Lipha
Section 3 A3.2.1/01	Curl, M	2004	The Calculation of Henry's Law Constant for chlorophacinone. TSGE laboratory report no. 12-1-12.HL Not GLP/Unpublished	Y	Lipha
Section 3 A3.3.1/01	Pesselman, R.	1990 b	Physical state determination of chlorophacinone (CPN). Hazleton Laboratories America, Inc., laboratory report no. HLA 6001-600. GLP/Unpublished.	Y	Lipha
Section 3 A3.3.2/01	Pesselman, R.	1990 c	Munsell color determination of chlorophacinone (CPN). Hazleton Laboratories America, Inc., laboratory report no. HLA 6001-599. GLP/Unpublished.	Y	Lipha
Section 3 A3.3.3/01	Pesselman, R.	1990 d	Odor determination of chlorophacinone (CPN). Hazleton Laboratories America, Inc., laboratory report no. HLA 6001-601. GLP/Unpublished.	Y	Lipha
Section 3 A3.4/01	Queche, P.	1999	NMR, MS, IR, UV/vis spectra. chlorophacinone active ingredient. Lipha s.a., laboratory report no. ASCLOR100-99. Not GLP/Unpublished.	Y	Lipha
Section 3 A3.5/01	Kramer, H., Marion, T	2002 b	Water solubility of chlorophacinone. Covance Laboratories Inc., laboratory report no. 6372-109. GLP/Unpublished.	Y	Lipha

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
Section 3 A3.5/02	Hoffman, M.	1988c	Water solubility determination of chlorophacinone. Hazleton Laboratories America, Inc., laboratory report no. HLA 6001-216. GLP/Unpublished.	Y	Lipha
Section 3 A3.6/01	Kramer, H., Marion, T	2002c	Octanol/water partition coefficient and dissociation constant of chlorophacinone. Covance Laboratories Inc., laboratory report no. 6372-111. GLP/Unpublished.	Y	Lipha
Section 3 A3.7/01	Pesselman, R.	1991	Solubility determination of chlorophacinone. Hazleton Laboratories America, Inc., laboratory report no. HLA 6372-100. GLP/Unpublished.	Y	Lipha
Section 3 A3.9/01	Loken, R.	1988	Octanol/water partition coefficient determination of chlorophacinone Hazleton Laboratories America, Inc., laboratory report no. HLA 6001-218. GLP/Unpublished.	Y	Lipha
Section 3 A3.9/02	Kramer, H., Marion, T	2002c	Octanol/water partition coefficient and dissociation constant of chlorophacinone. Covance Laboratories Inc., laboratory report no. 6372-111. GLP/Unpublished.	Y	Lipha
Section 3 A3.10/01	Lindemann, M.	2004a	Screening of the thermal stability in air of chlorophacinone. RCC Limited, laboratory report no. 849162. GLP/Unpublished.	Y	Lipha
Section 3 A3.11/01	Lindemann, M.	2004b	Determination of the flammability of chlorophacinone. RCC Limited, laboratory report no. 849161. GLP/Unpublished.	Y	Lipha
Section 3 A3.11/02	Lindemann, M.	2004c	Determination of the relative self-ignition temperature of chlorophacinone. RCC Limited, laboratory report no. 849160. GLP/Unpublished.	Y	Lipha
Section 3 A3.13/01	Lindemann, M	2003d	Determination of the surface tension of an aqueous solution of chlorophacinone. RCC Limited, report no. 849159. GLP/Unpublished.	Y	Lipha

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
Section 3 A3.15/01	Lindemann, M	2003e	Expert statement on the explosive properties of chlorophacinone. RCC Limited, laboratory report no. 849158. GLP/Unpublished.	N	Lipha
Section 3 A3.16/01	Lindemann, M	2003f	Expert statement on the oxidising properties of chlorophacinone. RCC Limited, laboratory report no. 849157. GLP/Unpublished.	N	Lipha
Section 4/ A4.1/01	Queche, P.	1997	Validation of the HPLC method for impurity determination. Chlorophacinone active ingredient Lipha SA, Report No. CLOVALIMP97. Non-GLP, Unpublished. *This report contains confidential information.*	Y	Lipha
Section 4/ A4.2(a)/01	Wolf, S.	2003a	Development and validation of the residue analytical method for chlorophacinone in soil. RCC Ltd., Report No. 849156. GLP, Unpublished.	Y	Lipha
Section 4/ A4.2(b)/01	Wolf, S.	2003b	Development and validation of a residue analytical method for chlorophacinone in air. RCC Ltd., Report No. 849155. GLP, Unpublished.	Y	Lipha
Section 4/ A4.2(c)/01	Wolf, S.	2003c	Development and validation of the residue analytical method for chlorophacinone in drinking and surface water. RCC Ltd., Report No. 849154. GLP, Unpublished.	Y	Lipha
Section 4/ A4.2(d)/01	Jones, A.	2004a	Validation of analytical methodology to determine bromadiolone, chlorophacinone and difethialone in blood. Central Science Laboratory, Report No. PGD-137. GLP, Unpublished.	Y	Lipha

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
Section 4/ A4.2(d)/02	Jones, A	2004 b	Validation of analytical methodology to determine bromadiolone, chlorophacinone and difethialone in liver. Central Science Laboratory, Report No. PGD-142. GLP, Unpublished.	Y	Lipha
Section 5/ A5.7.2/01	Anonymous	2003	RRAC (Rodenticide Resistance Action Committee), Checklist for rodenticide users experiencing difficulties. Not GLP, Published.	N	Public
Section 5/ A5.7.2/02	Anonymous	2003	Technical monograph 2003. Anticoagulant resistance management strategy for Pest Management professionals, Central and Local government and other competent users of rodenticides. CropLife International, Not GLP, Published.	N	Public
Section 6/ A 6.1.1-01	Mally C., and Porret-Blanc G.	1988	LD50 Evaluation of Chlorophacinone in Solution in PEG 300 Orally to Rats. Lipha Centre de Recherches, Lyon, France (Dates of experimental work: March 1, 1988- March 22, 1988). Unpublished report No.: 88.02.LM.91.RP2 GLP/Unpublished	Y	Lipha
Section 6/ A 6.1.1-02	Reagan E. L.	1986	Acute oral LD50 of Chlorophacinone in Beagle Dogs. Food and Drug Research Laboratories, Inc., Waverly, NY. FDRL study No: 9122A GLP/Unpublished	Y	Lipha
Section 6/ A 6.1.2-01	Lilja, H.S.	1990	Single Dose Dermal Toxicity Study (Range Finding I) Chlorophacinone. Toxicon Corporation, Woburn, MA. Laboratory report No: 89G-0146A GLP/Unpublished	Y	Lipha
Section 6/ A 6.1.2-02	Lilja, H.S.	1990	Single Dose Dermal Toxicity Study (Range Finding II) Chlorophacinone. Toxicon Corporation, Woburn, MA. Laboratory report No: 89G-0146B GLP/Unpublished	Y	Lipha

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
Section 6/ A 6.1.2-03	Lilja, H.S.	1990	Single Dose Dermal Toxicity Study (Range Finding III) Chlorophacinone. Toxicon Corporation, Woburn, MA. Laboratory report No: 89G-0146C. GLP/Unpublished	Y	Lipha
Section 6/ A 6.1.2-04	Lilja, H.S.	1990	Single Dose Dermal Toxicity Study (LD50 I) Chlorophacinone. Toxicon Corporation, Woburn, MA. Laboratory report No: 89G-0146D GLP/Unpublished	Y	Lipha
Section 6/ A 6.1.3-01	Holbert, M.S.	1991	Acute inhalation toxicity study of technical Chlorophacinone in rats. Stillmeadow, Inc., Sugar Land, Texas. Laboratory report No: 7436-90. GLP/Unpublished	Y	Lipha
Section 6/ A 6.1.4-01	Lilja, H.S.	1989	Primary Dermal Irritation Study. Chlorophacinone. Toxicon Corporation, Woburn, MA. Laboratory report No: 89G-0147. GLP/Unpublished	Y	Lipha
Section 6/ A 6.1.4-02	Lilja, H.S.	1989	Primary Ocular Irritation Study. Chlorophacinone. Toxicon Corporation, Woburn, MA. Laboratory report No: 89G-0148. GLP/Unpublished	Y	Lipha
Section 6/ A 6.1.5-01	Shapiro, R.	1990	EPA Guinea Pig Sensitisation (Buehler). Product Safety Labs, East Brunswick, NJ. Laboratory report No: T-9990. GLP/Unpublished	Y	Lipha
Section 6/ A 6.2-01	Belleville, M.J.		Absorption, distribution, metabolism and excretion studies in the rat using ^{14}C-labeled Chlorophacinone. Lipha S.A. Research Centre, Lyon, France. No laboratory study identification number. Non-GLP/Unpublished	Y	Lipha
Section 6/ A 6.2-02	Needham, D and Russell, N.	2004	[^{14}C]-Chlorophacinone: Metabolism in the rat following oral dosing. Covance Laboratories Ltd., UK. Laboratory report no. 2336/001-D1145 GLP/ Unpublished.	Y	Lipha

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
Section 6/ A 6.2-03	Hardwick, T. and Russell, N.	2003	[^{14}C]-Chlorophacinone: Rates of penetration through human skin using a flow through *in vitro* system. Covance Laboratories Ltd. Laboratory report No 2336/002-D1145 GLP/Unpublished	Y	Lipha
Section 6/ A 6.3.2-01	Fitzgerald G.B.	1990 a	Repeated Dose Dermal Toxicity: 21 Day Study – Sprague-Dawley Rats (Chlorophacinone). Toxicon Corporation, Woburn, MA. Laboratory report No: 90G-0726. GLP/Unpublished	Y	Lipha
Section 6/ A 6.3.2-02	Fitzgerald G.B.	1990 b	Repeated Dose Dermal Toxicity (21-Day) Study – New Zealand Albino Rabbits (Chlorophacinone). Toxicon Corporation, Woburn, MA. Laboratory report No: 90G-0727. GLP/Unpublished	Y	Lipha
Section 6/ A 6.3.2-03	Hamada, N.	1992 a	21-Day Dermal Toxicity Study in Rabbits with Chlorophacinone. Hazleton Washington Inc. Rockville, MD. Laboratory report No: HWA 2624-105 GLP/Unpublished	Y	Lipha
Section 6/ A 6.3.2-04	Hamada, N.	1992 b	21-Day Dermal Rangefinding Toxicity Study in Rabbits with Chlorophacinone. Hazleton Washington Inc. Rockville, MD. Laboratory report No: HWA 2624-106 GLP/Unpublished	Y	Lipha
Section 6/ A 6.3.2-05	Hamada, N.	1992 b	21-Day Dermal Rangefinding Toxicity Study in Rabbits with Chlorophacinone. Hazleton Washington Inc. Rockville, MD. Laboratory report No: HWA 2624-104 GLP/Unpublished	Y	Lipha
Section 6/ A 6.4.1-01	Mally, C., Porret-Blanc G and Lorgue, G.	1984	3 Month Toxicity Study on Rats by Oral Method Chlorophacinone (LM-91). Lipha Centre de Researches, Lyon, France. Laboratory report No: 84.05.LM.91.RPP GLP/Unpublished	Y	Lipha

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
Section 6/ A 6.6.1-01	Betbeder-Matibet A.	1981	Research on the Mutagenic Potential of Chlorophacinone Using the Ames Test. Lipha Bacteriology Laboratory, Centre de Recherches, Lyon, France. Laboratory report No: not stated Non-GLP/Unpublished	Y	Lipha
Section 6/ A 6.6.1-02	Lawlor, T.E.	1994	Mutagenicity Test with Chlorophacinone in the Salmonella – Escherichia coli/ Mammalian-Microsome Reverse Mutation Assay with a confirmatory Assay. Hazleton Washington Inc., Vienna, Virginia. Laboratory report No: HWA 16030-0409R GLP/Unpublished	Y	Lipha
Section 6/ A 6.6.2-01	Weill, N.	1990	Test to evaluate the Induction of Genic Mutations in CHO Cells (HGPRT Locus) Chlorophacinone. Hazleton France, France Laboratory report No: 006301. GLP/Unpublished	Y	Lipha
Section 6/ A 6.6.3-01	Stankowski, L. F.	1995	Structural Chromosomal Aberration Assay in Human Lymphocytes with Chlorophacinone (CPN). Pharmakon Research International, Inc., Waverly, PA. Laboratory report No: PH 324-LPT-001-94. GLP/Unpublished	Y	Lipha
Section 6/ A 6.6.4-01	Murli, H.	1994	Mutagenicity test on Chlorophacinone in an *in vivo* mouse micronucleus assay. Hazleton Washington Inc. Vienna, Virginia. Laboratory report No: HWA 16030-0-455CO. GLP/Unpublished	Y	Lipha
Section 6/ A 6.8.1-01	Tyl, R.W., Marr, M.C. and Myers, C.B	1994	Developmental toxicity Evaluation of Chlorophacinone Administered by Gavage to CD Sprague-Dawley Rats. Reproductive and Developmental Toxicology Laboratory, Research Triangle Institute, NC. Laboratory report No: 65C-5724-01/02. GLP/Unpublished	Y	Lipha

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
Section 6/ A 6.8.1-02	Tyl, R.W., Marr, M.C. and Myers, C.B	1994	Developmental toxicity Evaluation of Chlorophacinone Administered by Gavage to New Zealand White Rabbits. Reproductive and Developmental Toxicology Laboratory, Research Triangle Institute, NC. Laboratory report No:65C-5724-03/04. GLP/Unpublished	Y	Lipha
Section 6/ A 6.9-01	Depin, J.C. and Chavernac, G.	1986	LM 2219 Pharmacological approach. Research Centre, Lyonnaise Industrielle Pharmaceutique, 69359 Lyon Cedex, France. Report Number: No identification stated Non GLP/Unpublished	Y	Lipha
Section 6/ A 6.10-01	Markiewicz, V.R.	1991	Antidotal Treatment Study Following Oral Exposure to Chlorophacinone in Rats. Hazleton Washington Inc. Laboratory report No 2624-103. GLP/Unpublished	Y	Lipha
Section 6/ A 6.12.1-01	Bressot Perrin, H.	1999	Personal communication	N	Lipha
Section 6/ A 6.12.7-01	Anon.		Title: Principles of medical supervision of employees exposed to Difethialone, Bromadiolone and Chlorophacinone-vased rodenticides. Title: The treatment of anticoagulant rodenticide poisoning – Advice to physicians Personal communication	N	Lipha
Section 6/ A 6.13-01	Anon.		Title: The treatment of anticoagulant rodenticide poisoning – Advice to veterinarians	N	Lipha
Section 7/ A 7.1.1.1.1-01	Adam, D.	2003	^{14}C-Chlorophacinone: Hydrolysis at three different pH values. RCC Ltd., laboratory report no. 849153 GLP/Unpublished	Y	Lipha
Section 7/ A 7.1.1.1.2-01	Diehl, M.	2004	^{14}C-Chlorophacinone: Aqueous Photolysis Under Laboratory Conditions. RCC Ltd, Laboratory Report No. 948165 GLP/Unpublished).	Y	Lipha

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
Section 7/ A.7.1.1.2.1-01	Peither, A.	2003	Ready biodegradability of chlorophacinone in a manometric respirometry test. RCC Ltd., laboratory report no. 844816 GLP/Unpublished	Y	Lipha
Section 7/ A.7.1.3-01	Spare, W.	1993	Adsorption / desorption of chlorophacinone in four soil types. Agrisearch Inc., laboratory report no. 1416 GLP/Unpublished	Y	Lipha
Section 7/ A.7.2.1-01	Spare, W.	1994	Aerobic soil metabolism of chlorophacinone. Agrisearch Inc., laboratory report no. 1419 GLP/Unpublished	Y	Lipha
Section 7/ A.7.2.2.4-01	Spare, W.	1992	Soil photolysis of chlorophacinone. Agrisearch Inc., laboratory report no. 1418 GLP/Unpublished	Y	Lipha
Section 7/ A.7.3.1-01	Curl, M.G.	2003	The estimation of photochemical oxidative degradation of chlorophacinone. TSGE, laboratory report no. 12-1-12.POD Non GLP/Unpublished	Y	Lipha
Section 7/ A 7.4.1.1-01	Machado, M.W.	1992 a	Chlorophacinone - Acute toxicity to rainbow trout (*Oncorhynchus mykiss*) under flow-through conditions. Springborn Laboratories, Inc., report number 91-12-4025 GLP/Unpublished	Y	Lipha
Section 7/ A 7.4.1.1-02	Machado, M.W.	1992 b	Chlorophacinone - Acute toxicity to bluegill sunfish (*Lepomis macrochirus*) under flow-through conditions. Springborn Laboratories, Inc., report number 92-1-4079 GLP/Unpublished	Y	Lipha
Section 7/ A 7.4.1.2-01	Putt, A.E.	1992	Chlorophacinone - Acute toxicity to daphnids (*Daphnia magna*) under flow-through conditions. Springborn Laboratories, Inc., report number 91-11-3998 GLP/Unpublished	Y	Lipha

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
Section 7/ A 7.4.1.3-01	Peither, A.	2003 a	Toxicity of chlorophacinone to *Scenedesmus subspicatus* in a 72-hour algal growth inhibition test, RCC Ltd., report number 844814 GLP/Unpublished	Y	Lipha
Section 7/ A 7.4.1.4-01	Peither, A.	2003 b	Toxicity of chlorophacinone to activated sludge in a respiration inhibition test, RCC Ltd., report number 844817 GLP/Unpublished	Y	Lipha
Section 7/ A 7.5.1.2-01	Redgrave, V.A.	2000	Chlorophacinone: acute toxicity (LC_{50}) to the earthworm (*Eisenia foetida*). Huntingdon Life Sciences Ltd., report number LPA 196/002446 GLP/Unpublished	Y	Lipha
Section 7/ A7.5.3.1.1-01	Beavers, J.B.	1979	Acute oral LD_{50} - bobwhite quail. Chlorophacinone Wildlife International Ltd. Unnumbered report GLP/Unpublished	Y	Lipha
Section 7/ 7.5.3.1.1-02	Fletcher, D.W. and Pedersen, C.A.	1989 a	Chlorophacinone: 30-day acute oral LD_{50} study in bobwhite quail. Bio-Life Associates Ltd., report number 87 QD 106 GLP/Unpublished	Y	Lipha
Section 7/ 7.5.3.1.2-01	Fletcher, D.W. and Pedersen, C.A.	1989 b	Chlorophacinone: 30-day acute dietary LC_{50} study in bobwhite quail. Bio-Life Associates Ltd., report number 87 QC 105 GLP/Unpublished	Y	Lipha
Section 7/ 7.5.3.1.2-02	Fletcher, D.W. and Pedersen, C.A.	1989 c	Chlorophacinone: 30-day acute dietary LC_{50} study in mallard ducklings. Bio-Life Associates Ltd., report number 87 DC 103 GLP/Unpublished	Y	Lipha

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
Section 7/ 7.5.3.1.3-01	Riedel, B., Grün, G. and Clausing, P.	1990	Die subakute und subchronische Toxizität von Chlorophacinon an Japanwachteln (*Coturnix c. japonica*). Institut für Pflanzenschutzforschung Kleinmachnow der Akademie der Landwirtschaftswissenschaften der DDR – Ornithologische Forschungsstelle Seebach. Not GLP/Published: *Arch. exper. Vet.med., Leipzig*. **44** (3): pp 341-346	N	Public
Section 7/ 7.5.6-01	Baroch, J.	1997	Secondary hazard study using chlorophacinone-killed laboratory rats fed to black-billed magpies (*Pica pica*). Genesis Laboratories, Inc., report number 96004 GLP/Unpublished	Y	Lipha
Section 7/ 7.5.6-02	Ahmed, M.S., Baroch, J., Carlet, L. and Whaley, D.	1996	Secondary hazard study using chlorophacinone-killed laboratory rats fed to domestic ferrets (*Mustela putorius furo*). Genesis Laboratories, Inc., report number 96019 GLP/Unpublished	Y	Lipha

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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
Section 1			No study reports submitted		
Section 2			No study reports submitted		
Section 3/ B1 3.1.1-01	Lindemann, M.	2004 a	Determination of appearance (physical state, colour and odour) of chlorophacinone bloc. RCC Limited, laboratory report no. 849780. GLP/Unpublished.	Y	Lipha
Section 3/ B1 3.1.2-01	Lindemann, M.	2004 a	Determination of appearance (physical state, colour and odour) of chlorophacinone bloc. RCC Limited, laboratory report no. 849780. GLP/Unpublished.	Y	Lipha

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
Section 3/ B1 3.1.3-01	Lindemann, M.	2004 a	Determination of appearance (physical state, colour and odour) of chlorophacinone bloc. RCC Limited, laboratory report no. 849780. GLP/Unpublished.	Y	Lipha
Section 3/ B1 3.2-01	Lindemann, M.	2004 b	Expert Statement on the explosive properties of chlorophacinone moulded blocks (Loginet solide). RCC Limited, laboratory report no. 849777. Non GLP/Unpublished.	Y	Lipha
Section 3/ B1 3.3-01	Lindemann, M.	2004 c	Expert Statement on the oxidizing properties of chlorophacinone moulded blocks (Loginet solide). RCC Limited, laboratory report no. 849776. Non GLP/Unpublished.	Y	Lipha
Section 3/ B1 3.4-01	Lindemann, M.	2004 d	Determination of the relative self-ignition temperature of chlorophacinone bloc. RCC Limited, laboratory report no. 849774. GLP/Unpublished.	Y	Lipha
Section 3/ B1 3.4-02	Lindemann, M.	2004 e	Determination of the flammability of chlorophacinone bloc. RCC Limited, laboratory report no. 849775. GLP/Unpublished.	Y	Lipha
Section 3/ B1 3.5-01	Lindemann, M.	2004f	pH-determination of an aqueous dispersion of chlorophacinone bloc. RCC Limited, laboratory report no. 849778. GLP/Unpublished.	Y	Lipha
Section 3/ B1 3.6-01	Lindemann, M.	2004 g	Determination of the relative density of chlorophacinone bloc. RCC Limited, laboratory report no. 849779. GLP/Unpublished.	Y	Lipha

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
Section 3/ B1 3.7-01	Zobel, M.	2004 a	Determination of accelerated storage stability of Loginet Solide. Liphatech Inc., laboratory study no. 04008. GLP/Unpublished.	Y	Lipha
Section 3/ B1 3.7-02	Zobel, M.	2004 b	Protocol: Determination of the storage stability of Loginet Solide (shelf life at room temperature). Liphatech Inc., laboratory study no. 04009. GLP/Unpublished.	Y	Lipha
Section 4/ B1 4.1-01	Zobel, M.L	2004	Method validation: Analytical technique for the concentration of chlorophacinone in Loginet Solide. Liphatech Inc., laboratory report No 04007. GLP/Unpublished.	Y	Lipha
Section 5/ B1 5.10-01	Berny, P.	2003	Study on the efficacy of a block at 50 mg/kg of chlorophacinone in the rat, *Rattus Norvegicus*, wild strain, sensitive to warfarin. Laboratoire de Toxicologie, ENVL, laboratory report no.RE/0301/CPN/Block/Rn/S/T0 Non GLP/Unpublished	Y	Lipha
Section 6/ B1 6.1.1-01	Brunt, P.	2003 a	Loginet Solide: Acute Oral Toxicity in the Rat. Safepharm Laboratories Limited, Derbyshire, UK. Laboratory report no. 1840/012 GLP/Unpublished	Y	Lipha
Section 6/ B1 6.1.2-01	Brunt, P.	2003 b	Loginet Solide: Acute Dermal Toxicity (Limit test) in the Rat. Safepharm Laboratories Limited, Derbyshire, UK. Laboratory report no. 1840/013 GLP/Unpublished	Y	Lipha
Section 6/ B1 6.2-01	Brunt, P.	2003 c	Loginet Solide: Acute Dermal Irritation in the Rabbit. Safepharm Laboratories Limited, Derbyshire, UK. Laboratory report no. 1840/014 GLP/Unpublished	Y	Lipha
Section 6/ B1 6.2-02	Brunt, P.	2003 d	Loginet Solide: Acute Eye Irritation in the Rabbit. Safepharm Laboratories Limited, Derbyshire, UK. Laboratory report no. 1840/015 GLP/Unpublished	Y	Lipha

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
Section 6/ B1 6.3-01	Brunt, P.	2004	Loginet Solide: Skin sensitisation in the Guinea Pig. Safepharm Laboratories Limited, Derbyshire, UK. Laboratory report no. 1840/016 GLP/Unpublished	Y	Lipha
Section 6/ B1 6.6-01	Snowdon, P.J.	2003	Pilot study to determine primary sources of exposure to operators during simulated use of anticoagulant rodenticide baits. Synergy Laboratories Limited laboratory report no. SYN/1301 GLP/Unpublished	Y	Lipha
Section 6/ B1 6.6-02	Chambers, J.G., Snowdon, P.J.	2004	Study to determine potential exposure to operators during simulated use of anticoagulant rodenticide baits. Synergy Laboratories Limited laboratory report no. SYN/1302 GLP/Unpublished	Y	Lipha
Section 7			No study reports submitted		

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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
Section 1			No study reports submitted		
Section 2			No study reports submitted		
Section 3/ B2 3.1.1-01	Lindemann, M.	2004 a	Determination of appearance (physical state, colour and odour) of chlorophacinone wheat. RCC Limited, laboratory report no. 849792. GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.1.2-01	Lindemann, M.	2004 a	Determination of appearance (physical state, colour and odour) of chlorophacinone wheat. RCC Limited, laboratory report no. 849792. GLP/Unpublished.	Y	Lipha

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
Section 3/ B2 3.1.3-01	Lindemann, M.	2004 a	Determination of appearance (physical state, colour and odour) of chlorophacinone wheat. RCC Limited, laboratory report no. 849792. GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.2-01	Lindemann, M.	2004 b	Expert Statement on the explosive properties of chlorophacinone wheat (Caid appats). RCC Limited, laboratory report no. 849795. Non GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.3-01	Lindemann, M.	2004 c	Expert Statement on the oxidizing properties of chlorophacinone wheat (Caid appats). RCC Limited, laboratory report no. 849796. Non GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.4-01	Lindemann, M.	2004 d	Determination of the relative self-ignition temperature of chlorophacinone wheat. RCC Limited, laboratory report no. 849798. GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.4-02	Lindemann, M.	2004 e	Determination of the flammability of chlorophacinone wheat. RCC Limited, laboratory report no. 849797. GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.5-01	Lindemann, M.	2004f	pH-determination of an aqueous dispersion of chlorophacinone wheat. RCC Limited, laboratory report no. 849794. GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.6-01	Lindemann, M.	2004 g	Determination of the bulk density of chlorophacinone wheat. RCC Limited, laboratory report no. 849793. GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.7-01	Lindemann, M.	2004 h	Accelerated storage stability of chlorophacinone wheat. RCC Limited, laboratory report no. 849803. GLP/Unpublished.	Y	Lipha

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
Section 3/ B2 3.7-02	Gambert, C.	2003	Stability study: chlorophacinone red wheat at 50 mg/kg. Liphatech SAS, laboratory report no. STAB CLO 191. Non GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.7-03	Lindemann, M.	2004i	Study plan: Determination of the storage stability of chlorophacinone wheat (shelf life at room temperature). RCC Limited, laboratory report no. 849802. GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.8-01	Lindemann, M.	2004j	Determination of the flowability of chlorophacinone wheat. RCC Limited, laboratory report no. 849801. GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.8-02	Lindemann, M.	2004 k	Determination of dust content of chlorophacinone wheat. RCC Limited, laboratory report no. 849800. GLP/Unpublished.	Y	Lipha
Section 3/ B2 3.8-03	Lindemann, M.	2004l	Determination of dustiness of chlorophacinone wheat. RCC Limited, laboratory report no. 849799. GLP/Unpublished.	Y	Lipha
Section 4/ B2 4.1-01	Lindemann, M.	2004	Validation of an analytical method for the determination of chlorophacinone in chlorophacinone wheat. RCC Limited, laboratory report no. 849804. GLP/Unpublished	Y	Lipha
B2 5.10-01	Lorgue, G.	1999.	Study on the efficacy and attractivity of a wheat bait based on chlorophacinone in the Norway rat, wild strain, Rattus Norvegicus. Laboratoire de Toxicologie, ENVL, laboratory report no. P.9903 Non GLP/Unpublished	Y	Lipha

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
B2 5.10-02	Berny, P.	2003	Study on the efficacy and attractivity of a wheat bait at 50 mg/kg of chlorophacinone in the rat, Rattus Norvegicus, wild strain, sensitive to coumafene. Laboratoire de Toxicologie, ENVL, laboratory report no. RE/0302/CPN/Wheat/Rn/S/T0 Non GLP/Unpublished	Y	Lipha
B2 5.10-03	Berny, P.	2003	Study on the efficacy and attractivity of an impregnated wheat bait with 50 mg/kg of chlorophacinone in the house mouse, *Mus musculus*, wild strain, sensitive to warfarin. Laboratoire de Toxicologie, ENVL, laboratory report no. RE/0303/CPN/Wheat/Mm/S/T0. Non GLP/Unpublished	Y	Lipha
Section 6/ B2 6.1.1-01	Myers, R.C. and Christopher, S.M.	1994 a	Rozol® Pellets: Acute Peroral Toxicity Study in the Rat. Bushy Run Research Center. Laboratory report no. 93N1275 GLP/Unpublished	Y	Lipha
Section 6/ B2 6.1.2-01	Glaza, S.M.	1995 a	Acute Dermal Toxicity Study (Limit Test) of Rozol® Pocket Gopher Bait in Rabbits. Hazleton Wisconsin, Madison, Wisconsin, USA. Laboratory report no. HWI 41200819 GLP/Unpublished	Y	Lipha
Section 6/ B2 6.1.2-02	Parker, R.M.	1992	Dermal limit study of Rozol® Paraffinised Pellets administered to New Zealand White Rabbits. TSI Redfield Laboratories. Laboratory report no. 008-0005 GLP/Unpublished	Y	Lipha
Section 6/ B2 6.2-01	Glaza, S.M.	1995 b	Primary Dermal Irritation Study of Rozol® Pocket Gopher Bait in Rabbits. Hazleton Wisconsin, Madison, Wisconsin, USA. Laboratory report no. HWI 41200820 GLP/Unpublished	Y	Lipha

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
Section 6/ B2 6.2-02	Glaza, S.M.	1995 c	Primary Eye Irritancy Study Rozol® Pocket Gopher Bait in Rabbits. Hazleton Wisconsin, Madison, Wisconsin, USA. Laboratory report no. HWI 41200821 GLP/Unpublished	Y	Lipah
Section 6/ B2 6.2-03	Myers, R.C. and Christopher, S.M.	1993 a	Rozol® Pellets: Cutaneous Irritancy Testing using the Rabbit. Bushy Run Research Center. Laboratory report no. 93N1306A GLP/Unpublished	Y	Lipha
Section 6/ B2 6.2-04	Myers, R.C. and Christopher, S.M.	1993 b	Rozol® Pellets: Ocular Irritancy Testing using the Rabbit. Bushy Run Research Center. Laboratory report no. 93N1306B GLP/Unpublished	Y	Lipha
Section 6/ B2 6.3-01	Glaza, S.M.	1995 d	Dermal sensitization Study of Rozol® Pocket Gopher Bait in Guinea Pigs – Closed patch Technique. Hazleton Wisconsin, Madison, Wisconsin, USA. Laboratory report no. HWI 41200822 GLP/Unpublished	Y	Lipha
Section 6/ B2 6.3-02	Myers, R.C. and Christopher, S.M.	1994 b	Rozol® Pellets: Dermal Sensitization Study in the Guinea Pig Using the Buehler Technique. Laboratory report no. 93N1307. GLP/Unpublished	Y	Lipha
Section 6/ B2 6.6-01	Snowdon, P.J.	2003	Pilot study to determine primary sources of exposure to operators during simulated use of anticoagulant rodenticide baits. Synergy Laboratories Limited laboratory report no. SYN/1301 GLP/Unpublished	Y	Lipha
Section 6/ B2 6.6-02	Chambers, J.G., Snowdon, P.J.	2004	Study to determine potential exposure to operators during simulated use of anticoagulant rodenticide baits. Synergy Laboratories Limited laboratory report no. SYN/1302 GLP/Unpublished	Y	Lipha
Section 7			No study reports submitted		