Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Renewal of approval

Assessment Report

Flocoumafen

Product-type 14
(Rodenticide)

September 2016

eCA: NL

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 the active substance flocoumafen as product-type 14 (rodenticides), carried out in the context of evaluation of applications for renewal provided for in Article 14 of the Biocidal Product Regulation (EU) No 528/2012 (BPR), with a view to the possible renewal of the approval of this substance.

With the intention to streamline the renewal of substance approvals and product authorisations of anticoagulant rodenticides[1] and their comparative assessments, at the 50th CA meeting the document "Substance approval and product authorisation renewals of the anticoagulant rodenticides" (CA-Feb13-Doc.5.2.b – Final) was endorsed. This was confirmed at the 61th CA meeting laid down in the document "Renewal of anticoagulant rodenticides active substances (CA-Sept15-Doc.5.3).

A workshop was held in Brussels on 26 February 2015 regarding the report on *Risk mitigation measures for anticoagulant rodenticides as biocidal products (Final Report October 2014; ISBN 978-92-79-44992-5)* prepared for the European Commission. The revised summary of the workshop was endorsed at the 62nd CA meeting (CA-Nov15-Doc.5.4). The BPC Efficacy Working Group discussed in WGI-2016 some recommendations of the RMM report for anticoagulant rodenticides.

Flocoumafen was approved as an existing active substance, in product-type 14 under the Biocidal Products Directive (Inclusion Directive 2009/150/EC). The renewal of the active substance has been requested by BASF Nederland B.V. on behalf of BASF Agro B. V. Arnhem (NL) Zürich Branch.

On 7th of July 2015, the Netherlands competent authority (eCA) received a dossier from BASF Nederland B.V. on behalf of BASF Agro B. V. Arnhem (NL) Zürich Branch. The eCA accepted the dossier as complete for the purpose of the evaluation on 16th of July 2015. On the basis of the available information the eCA decided that only a limited evaluation in accordance with Article 14(2)(2) of the BPR of the application is necessary.

As all anticoagulant rodenticides meet the exclusion criteria. If approved, stringent risk mitigation measures will need to be applied. Where no new information was available in the application of renewal, the revision of the evaluation applying current guidance is postponed to product authorisation. This decision shall exclusively apply for the renewal of anticoagulant rodenticides. On the 25th of March 2016, the eCA submitted to the Agency and the applicant the assessment report.

In order to review the assessment report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by ECHA. Revisions agreed upon were presented at the 16th Biocidal Products Committee and its Environment Working Group meeting (WGI-2016) the assessment report was amended accordingly.

1.2. Purpose of the assessment report

The aim of the assessment report is to support the opinion of the Biocidal Products Committee and the decision on the renewal of the approval of Flocoumafen for product-type 14, and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

[1] The concerned active substances are: brodifacoum, bromadiolone, chlorophacinone, coumatetralyl, difethialone, difenacoum, flocoumafen and warfarin.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available from the Agency web-site shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Regulation (EU) No 528/2012, such conclusions may not be used to the benefit of another applicant, unless access to these data for that purpose has been granted to that applicant.

2. OVERALL SUMMARY AND CONCLUSIONS[2]

2.1. Presentation of the Active Substance

2.1.1. Identity

Substance specification

The identity has not been re-evaluated. Please refer to appendix I (List of Endpoints) for data on the identity of flocoumafen.

Although a reference specification is available for flocoumafen, it has not been set using the agreed statistical approach. The original reference source included in the CA report was withdrawn and replaced by a new source, evaluated by the eCA (report October 2010). The new source was considered equivalent to the reference source. It also resulted in addition of a new impurity to the reference specification, which was proven to be present in the original reference source as well by re-analysis of batches from the reference source.

Based on the agreements made during the WebEx conference of November 2015, the applicant should submit QC data to confirm the specification. The most recent batch analysis was performed in 2010 (< 10 years old study). A date of submission was not yet discussed or agreed on.

ISO common name

In the original competent authority report, it was indicated that the ISO common name for flocoumafen cannot apply using the specified upper and lower ranges of the cis and trans isomers (50-80% cis, 20-50% trans), and that it should be amended. The ISO common name has not yet been amended, however.

2.1.2. Intended Uses

The intended uses have not changed since the original approval. Flocoumafen is intended to be used for the control of commensal rodents (Rattus norvegicus, Rattus rattus, and Mus musculus) in and around buildings, animal housings, or food stores. The intended users are professionals (trained and non-trained) and general public.

Below details on the intended use are summarised.

Table 2.1.2-1: Summary of the intended use data of the active substance flocoumafen (wax block, 0.005% flocoumafen):

[2] See document CA-Sept15-Doc.5.3 - Renewal anticoagulant rodenticides.doc

MG/PT	Field of use envisaged	Organisms controlled	Application type	Conc (w/w)
MG 03/ PT 14	Pest control/ Rodenticides	Rats (in and around buildings) and mice (in buildings)	User category – Professional and Non-professional, Method - Manual application, Application aim – Control, Type of formulation – bait (ready for use).	0.005% ≡ 0.05g/kg≡50 ppm

2.2. Summary of the Assessment

2.2.1. Specification of the different sources of the active substances

No data was provided to confirm the specification of the active substance. This will be addressed in a separate procedure. See section 2.1.1 for more information.

2.2.2. Assessment as to whether the conclusion of the initial assessment of approval remain valid

2.2.2.1. Physico-chemical properties and methods of analysis

No new data on the physical and chemical properties and the post-registration analytical methods for monitoring of flocoumafen was provided.

2.2.2.2. Classification and Labelling

Flocoumafen presently has a harmonised classification according to Regulation (EC) No 1272/2008 (CLP Regulation) with H300/H310/H330 'Fatal if swallowed, in contact with skin or if inhaled', H372 'Causes damage to the blood through prolonged or repeated exposure' and H410 'Very toxic to aquatic life with long lasting effects'.

The committee for Risk Assessment (RAC) has published the opinion on the classification and labelling of flocoumafen (d.d. 14 March 2014). Flocoumafen was discussed together with a group of eight anti-vitamin K rodenticides (Coumatetralyl (Denmark), Difenacoum (Finland), Warfarin (Ireland), Brodifacoum (Italy), Flocoumafen (The Netherlands), Difethialone (Norway), Chlorophacinone (Spain) and Bromodialone (Sweden).

Based on the RAC Opinion (d.d. 14 March 2014) Flocoumafen warrants the following classification:

- Acute Tox. 1 H300 (criterion: LD_{50}, oral, rat $\leq$ 5 mg/kg) based on the oral LD_{50} for rats (range from 0.13-0.5 mg/kg bw)
- Acute Tox. 1 H310 (criterion: LD_{50}, dermal, rat or rabbit $\leq$ 50 mg/kg) based on the dermal LD_{50} for rats (range from 0.43-1.14 mg/kg bw)
- Acute Tox. 1 H330 (criterion: LD_{50}, inhalation, rat, for dusts and mists $\leq$ 0.05 mg/l/4h) based on the inhalatory LD_{50} values of 0.0006-0.002 mg/l/4h for the mouse and 0.0008-0.007 mg/l/4h for the rat (both sexes combined)
- STOT RE 1; H372 stating the blood as the main affected organ: H372: "Causes damage to the blood through prolonged or repeated exposure". Death of all exposed animals due to anticoagulation effect of Flocoumafen was observed in the 90-day rat study at levels (0.0125 and 0.03 mg/kg bw/day) (key study) which is well below the CLP criterion of "oral, rat $\leq$ 10 mg/kg bw/day for 90-days" used for classification with STOT RE 1; H372. SCLs were set for STOT RE 1; H372 above 0.05% and STOT RE 2; H373 between 0.005 and 0.05%.

- Repr. 1B; H360D. Based on the known developmental toxicity of the AVK rodenticide Warfarin in humans (Repr 1A),the reproductive toxicity of Flocoumafen has been analysed in detail. It is acknowledged that the animal developmental toxicity studies on Warfarin are weakly positive and that the animal developmental toxicity studies on Flocoumafen are negative. The evaluation of developmental effects of all 2nd generation AVK rodenticides is difficult as repeated exposure to relatively low doses during gestation lead to maternal toxicity and lethality. Thus renders the detection of developmental toxicity at higher doses not possible. Based on the assumption that all AVK rodenticides, including Warfarin and other anticoagulant coumarin-based pharmaceuticals share the same MoA, namely inhibition of vitamin K epoxide reductase (VKOR), the assessment of Flocoumafen includes consideration of the total database for the AVKs. A weight of evidence assessment resulted in the conclusion that Flocoumafen has the capacity to adversely affect the human *in utero* development. Therefore a classification as Repr. 1B is proposed. As the other AVK rodenticides are equally or more toxic than Warfarin, it is not considered appropriate to apply the generic concentration limit for these substances (0.3%), but rather to base the SCLs on the SCL proposed for Warfarin. Thus, the RAC is of the opinion that the SCL for Warfarin can be used as a surrogate SCL for the other AVK rodenticides, resulting in a SCL of 0.003% for all the currently discussed AVK rodenticides, including Flocoumafen.
- Aquatic Acute 1 (H400) with an M-factor of 10 and Aquatic Chronic 1 (H410) with an M-factor of 10. The lowest aquatic acute toxicity value was an LC_{50} of 0.07 mg/l in *Oncorhynchus mykiss* (OECD 203). This value is ≤ 1 mg/l, therefore Flocoumafen classifies as Acute category 1 (H400) with a M-factor of 10, because the LC_{50} is between 0.01 and 0.1 mg/l. No adequate chronic data was available for all three trophic levels and only chronic data from algae were submitted in the CLH report. According to this, no classification would result for Flocoumafen based on a NOE_rC > 18.2 mg/L. However, the surrogate approach should be applied due to the lack of chronic data for fish and invertebrates. Taking into account the fact that the substance is not rapidly degradable, the log K_{ow} ≥ 4 and the LC_{50} (fish) ≤ 0.1mg/L (0.07 mg/L), classification as Aquatic Chronic 1 (H410) with an M- factor of 10 is justified.

For further details we refer to RAC opinion and the background document:

http://echa.europa.eu/documents/10162/13626/rac_clh_opinion_flocoumafen_adopted_en.pdf
http://echa.europa.eu/documents/10162/13626/rac_clh_bd_flocoumafen_en.pdf

The resulting Annex VI entry, if agreed by COM (draft 9th ATP to CLP), is listed below:

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Repr. 1B; H360D Acute Tox. 1; H300 Acute Tox. 1; H310 Acute Tox. 1; H330 STOT RE1; H372 (blood) Aquatic Acute 1; H400 Aquatic Chronic1; H410
Labelling	
Pictograms	GHS06 GHS08 GHS09
Signal Word	Danger
Hazard Statement Codes	**H360D**: May damage the unborn child **H300**: Fatal if swallowed

	H310: Fatal in contact with skin **H330**: Fatal if inhaled **H372**: Causes damage to the blood through prolonged or repeated exposure **H410**: Very toxic to aquatic life with long lasting effects
Suppl. Hazard statement Code(s)	-
Specific Concentration limits, M-Factors	Repr. 1B; H360D: C ≥ 0,003 % STOT RE 1; H372: C ≥ 0,05 % STOT RE 2; H373: 0,005 % ≤ C < 0,05 % M =10 for Aquatic Acute toxicity M =10 for Aquatic Chronic toxicity

2.2.2.3. Efficacy and resistance

No new information on the efficacy is available since the original approval. The conclusions on the efficacy will therefore remain the same. According to the applicant to date, no incidences of resistance towards flocoumafen are known. This is in line with scientific evidence as referenced in the report on RMM for anticoagulant rodenticides[3] where it is stated that 'there is no evidence of field resistance to brodifacoum, difethialone and flocoumafen'. However, given the resistance development against FGARs and less potent SGARs and the similar mode of action of the anticoagulant rodenticides, resistance development should be carefully monitored. It was therefore concluded at WG EFF that appropriate data for resistance monitoring should be provided by the applicants during the next renewal process depending on the feasibility of the implementation of a harmonised resistance monitoring programme at EU level. This has been added as a requirement of further information at 2.3.4.

2.2.2.4. Human health assessment

No new information is available since the original approval. However, the exposure calculation performed in the original approval report are done based on a worst-case assumptions for the number of application/handling bait stations. The number of applications are harmonised in HEEG opinion 12 on the Harmonised approach for the assessment of rodenticides (anticoagulants). As the exposure calculation in the original report were already worst-case, the final conclusion on the safe use of flocoumafen for the protected (gloves) professional user and unprotected general public remains valid. At product authorisation new exposure calculations should be performed taking into account the number of applications in HEEG opinion 10 and 12.

2.2.2.5. Environmental assessment

Five studies were submitted, that were not part of the Annex I review:

- Wenzel A. (2011): Fish, bioconcentration of Flocoumafen according to the OECD Guideline 305 and EU method C.13
- Simon, M. (2007): Soil microorganisms: Effects of Flocoumafen on nitrogen and carbon transformation.
- Simon, M. (2007): Earthworm acute toxicity test: acute toxicity of Flocoumafen on *Eisenia fetida*.
- Simon, M. (2007): Terrestrial plants, growth test: Effect of Flocoumafen on the seedling emergence and growth of *Avena sativa, Lactuca sativa, Phaseolus aureus, Raphanus sativus, Sinapis alba*, and *Triticum aestivum.*

[3] Available at https://circabc.europa.eu/w/browse/d66ad096-37a1-4903-a3e0-24607ca3f3ea

- Simon, M. (2012): Bioaccumulation in Terrestrial Oligochaetes - Uptake and elimination of Flocoumafen in *Eisenia fetida*

RMS considers all new studies acceptable, except the earthworm (*Eisenia fetida* bioncentration study as explained below.

The applicant has submitted a study in which bioaccumulation in the earthworm *Eisenia fetida* was investigated. The study was conducted according to the principles of GLP and according to the OECD 317 guideline without deviations. The following was concluded:

- BSAF[a, b] (biota to soil accumulation factor) at steady state conditions (Ca/Cs): 2.41
- BASF based on kinetics (ks/ke) 3.04

All partitioning coefficients are expressed as dry weight soil to dry weight worm.

The applicant has stated that equilibrium was reached within a couple of days. This statement contradicts with the derived uptake (2.07/d) and elimination (0.642/d) rate constants using a two-compartment model (Table 5) that suggest equilibrium around ten days. Although the elimination rate constant (k_e) was fitted with high accuracy (r^2=0.966), the uptake rate constant (k_s) could not be derived properly (r^2=0.285). Consequently, the 95% confidence intervals (not reported) for both k_s and the BSAF are expected to be large.

The poor uptake kinetics could be explained by non-equilibrium conditions. Most likely, the worms have depleted the pore water phase after one day, which was not quickly enough replenished by desorption of the active substance from the soil matrix as desorption is a slow process especially in static systems such as soils. In other words, equilibrium is not determined by uptake kinetics in worms, but to desorption from the soil matrix. Another explanation may be the extraction methods applied. The eCA wonders if an extraction with dichloromethane:acetone by shaking is sufficient for hydrophobic compounds such as Flocoumafen as the amount of non-extractable radioactivity (NER) in worm tissues was up to 50% in some samples. Soxhlet extraction, for instance, with a more hydrophobic solvent such as hexane would have result in higher extraction efficacies. Nevertheless, as BSAFs were based on total concentrations in worms including metabolites and NER, the extraction technique applied would have only a minor effect on the obtained BSAF values.

Due to the presumed non-equilibrium conditions and the uptake rate constant that could not be derived accurately, the eCA is on the opinion that the derived values are not applicable for the environmental risk assessment as the expected variation is too large. Nevertheless, the submitted study has demonstrated that actual bioaccumulation is clearly lower than QSAR-predicted values as flocoumafen is rapidly eliminated from earthworms.

Minor comments:

- the water holding capacity (WHC) and/or moisture contents of the soil applied was not mentioned;
- 95% confidential intervals for the uptake and elimination rate constants were not reported.

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[a] The terms applied in the study report lead to confusions as, according to van Leeuwen and Vermeire (ref 1), the bioconcentration factor (BCF) is equal to the bioaccumulation factor (BAF). Both representing the uptake of hydrophobic chemicals from the surrounding water or pore water phase. However, when additional uptake via the digestive system cannot be excluded, (e.g. filter feeders, ingestion of soil particles, etc) the term bioconcentration factor cannot be used as it represents passive partition from water to animal lipid. Because the presented partitioning coefficient was expressed as the concentration in worms divided by the concentration in soils, the term 'biota to soil accumulation factor (BSAF)' is more appropriate.

[b] Because no BCFs or BAFs were derived, formula 82c of the TGD has to be adjusted accordingly. $BCF_{earthworm}$ and $C_{porewater}$ must be replaced by BSAF and C_{soil}, respectively.

Ref 1:van Leeuwen, C.J., Vermeire, T.G. (editors). 2007. Risk Assessment of Chemicals: An Introduction. 2nd edition.Springer, Dordrecht, The Netherlands.

Below the four accepted studies are briefly summarised:

Soil microorganisms:	EC_{10} 12.1 mg/kg dry soil or 10.7 mg/kg wet soil (nitrogen mineralization) EC_{50} > 1000 mg/kg dry soil or 882.4 mg/kg wet soil (nitrogen mineralization) NOEC > 1000 mg/kg dry soil or 882.4 mg/kg wet soil (carbon mineralization) EC_{50} > 1000 mg/kg dry soil or 882.4 mg/kg wet soil (carbon mineralization)
Earthworms:	EC_{50} > 1000 mg/kg dry soil or 882.4 mg/kg wet soil
Plants:	EC_{50} ≥ 714 mg/kg dry soil or 630.0 mg/kg wet soil NOEC = 179 mg/kg dry soil or 157.9 mg/kg wet soil
Bioconcentration in fish:	BCF_{fish} (kinetic) = 24,300 L/kg wwt

The endpoints of these studies do not affect the outcome of the assessment, the AR has not been amended. These points, however, should be taken into account during product authorisation.

2.2.2.6. Fate and distribution in the environment

No new information is available and the conclusions of the CAR (May 2009) for flocoumafen (PT14) drawn in the fate and distribution section remain the same. However, in the original CAR the risk for groundwater was not assessed. This should be amended in the renewal process.

2.2.2.7. PBT and POP assessment

PBT assessment

Substances that fulfil the PBT or vPvB criteria shall not be included in the Union list of approved substances unless releases to the environment can be effectively prevented.

Since December 2010 it is agreed that the PBT assessment is carried out on basis of the criteria set out under Regulation (EC) No. 1907/2006.

Persistence

The following information on degradation / transformation in water is available:

Flocoumafen has been shown to be hydrolytically stable under environmentally relevant conditions (DT50 > 1 year).

Flocoumafen is not readily biodegradable and does not degrade under anaerobic conditions.

Flocoumafen was found to be susceptible to photo-transformation in water (DT50 = 1.67 d). Transformation products could be identified partially as 4-hydroxy-3-[3-(4-hydroxyphenyl)-1,2,3,4-tetrahydro-1-naphthyl]coumarin and 4-(Trifluoromethyl)-benzoic acid.

Information on degradation rates in water and sediments (freshwater and marine) is lacking. However, based on the low biodegradation potential in soil (DT50 = 213 days at 20°C) and the

high hydrolytical stability flocoumafen is considered to be very persistent in water and sediment.

Bioaccumulation

In a bioconcentration study in fish a BCF of 24,300 L/kg based on whole body wet weight is determined. From the BCF value of flocoumafen it can be concluded that the active substance is very bioaccumulative.

Toxicity

Long-term exposure of the aquatic environment to flocoumafen is not expected. A prolonged toxicity study in fish is not considered to be required. A chronic NOEC of flocoumafen for marine or freshwater organisms is not available. Lowest acute toxicity was observed with a fish species (*Oncorhynchus mykiss*). LC50(4d) = 0.07 mg/L. Extrapolation to a chronic NOEC would result in 0.007 mg/L (extrapolation factor 0.1). Conclusion chronic toxicity <0.01 mg/L (T criterion).

There are no indications that flocoumafen has endocrine disruptive effects. Based on CMR data, flocoumafen is considered to be non-genotoxic (see Doc IIA, chapter 3.6, final CAR). Therefore, and since there is a risk that animals bleed to death during labour the performance of a two-generation reproduction study might cause unnecessary harm to laboratory animals, it is concluded that a carcinogenicity study with flocoumafen is not considered necessary (see Doc IIA, chapter 3.7 of final CAR of flocoumafen).

Teratogenity:

Based on the known developmental toxicity of the AVK rodenticide Warfarin in humans (Repr 1A),the reproductive toxicity of Flocoumafen has been analysed in detail. It is acknowledged that the animal developmental toxicity studies on Warfarin are weakly positive and that the animal developmental toxicity studies on Flocoumafen are negative. The evaluation of developmental effects of all 2nd generation AVK rodenticides is difficult as repeated exposure to relatively low doses during gestation lead to maternal toxicity and lethality. Thus renders the detection of developmental toxicity at higher doses not possible. Based on the assumption that all AVK rodenticides, including Warfarin and other anticoagulant coumarin-based pharmaceuticals share the same MoA, namely inhibition of vitamin K epoxide reductase (VKOR), the assessment of Flocoumafen includes consideration of the total database for the AVKs. A weight of evidence assessment resulted in the conclusion that Flocoumafen has the capacity to adversely affect the human in utero development. Therefore a classification as Repr. 1B, H360D is proposed.

Fertility:
No multigeneration study investigating a potential effect of flocoumafen on fertility was available but effects on reproductive organs have been observed in other studies. In a single dose study with female rats, effects on ovaries and fertility were observed, however, at doses close to the LD50 values and possibly causing internal bleedings. In a 90-day rat study, haemorrhages were observed in male reproductive organs (testes, prostate, epididymes), but not in female ovaries. But also in this study the effects were noted at doses that caused severe generalised toxicity and death. Since the effects observed in female (single dose) and male rats (repeated dose) could be related to the anticoagulation and were neither specific nor restricted to the reproductive system (effects secondary to severe generalised toxicity, i.e. haemorrhages, death), the data on flocoumafen do not meet the criteria for classification for fertility under Regulation EC 1272/2008. The structural analogue warfarin did not show any effect on fertility after many years of human use and neither in a two generation reproduction study in rats with vitamin-K supplementation. It has therefore no classification for fertility. Overall, there is insufficient evidence for a potential effect of flocoumafen on fertility, so no classification is proposed.

Overall conclusion is that flocoumafen fulfils the T criterion.

It is concluded that flocoumafen should be considered a PBT and vPvB substance.

POP assessment

Protection goals and risk management of the UN-ECE POPs Protocol are control, reduction or elimination of discharges, emissions and losses of POPs. The following P (persistent) O (organic) P (pollutants) criteria are laid down in Executive Body decision 1998/2.

	POPs-criteria
Long-range transport potential	Vapour pressure <1000 Pa and half-life in air > 2 days or monitoring data in remote area showing that the substance is found in remote regions
Toxicity (1)	Potential to adversely affect human health and/or environment
Persistence	Half-life in water > 2 months or in sediment >6 months or in soils > 6 months
Bioaccumulation	(i) BCF or BAF >5000 or log Pow > 5 (ii) Alternatively, if the bio-accumulative potential is significantly lower than (i) above, other factors, such as the high toxicity of the substance, that make it of concern within the scope of the protocol.

(1) L(E)C50; NOEC - no observed effect concentration; CMR - carcinogenic, mutagenic or toxic to reproduction.

Considering that the vapour pressure of flocoumafen is < 1 x 10^{-3} Pa (1.33 10^{-10} Pa at 25°C estimated with EPIWIN) combined with a calculated half-life in air of 0.185 days, based on reaction with hydroxyl radicals (0.5x10^6 OH/cm^3; 24-h day time) the criterion for long-range transport potential not is fulfilled.

Flocoumafen is not readily biodegradable and does not degrade under anaerobic conditions. Flocoumafen was found to be susceptible to photo-transformation in water (DT50 = 1.67 d). Transformation products could be identified partially as 4-hydroxy-3-[3-(4-hydroxyphenyl)-1,2,3,4-tetrahydro-1-naphthyl]coumarin and 4-(Trifluoromethyl)-benzoic acid.

Information on degradation rates in water and sediments (freshwater and marine) is lacking. However, based on the low biodegradation potential in soil (DT50 = 213 days at 20°C) and the high hydrolytical stability flocoumafen is considered to be very persistent in water and sediment. The Persistence criterion is fulfilled.

POPs Toxicity criteria are not clearly defined, but considering the lowest acute LC50 of flocoumafen for fish is of 70 µg/L the Toxicity criterion is met.

The experimentally derived BCF for fish is 24,300 L/kg ww, hence > 5000, and the log Pow is > 5, thus the Bioaccumulation criterion is met.

Conclusion for the POP characterisation:

On basis of the available can be concluded that the initial criteria for long-range transport potential are not met. Therefore this substance is not a POPs candidate.

2.2.2.8. Assessment of endocrine disruptor properties

No new information is available and the conclusions of the Assessment Report (May 2009) for flocoumafen (PT14) drawn in the PBT assessment section on endocrine disruptive properties remain the same.

2.2.3. Assessment of the recommendations arising from the report[4] on RMM for antiocoagulant rodenticides that are relevant for the active substance.

- For rat control, FGARs and less potent SGARs should always be considered as the first choice. SGARS should only be used against rats, where there is evidence that infestations are resistant.
Ideally where the resistance status is known prior to treatment, products containing the least potent active substance that will effect complete control should be used first, i.e.non-chemical methods > FGARs > less potent SGARs > potent SGARs. The authorisation of biocidal products should be decided upon the national or regional resistance situation. However, often this resistance status is not known. A harmonised programme to rapidly determine the resistance status of a rodent infestation prior to treatment should be developed. Currently such a programme is not available, but is under development. Given the uncertainties about the protocol to be used, the resources, data collection and sharing, etc. at the time of this renewal it was concluded at WG EFF that appropriate data for resistance monitoring should be provided by the applicants during the next renewal process depending on the feasibility of the implementation of a harmonised resistance monitoring programme at EU level. This has been added as a requirement of further information at 2.3.4.

- For mouse control, SGARs should always be considered as the first choice, as FGARs have low efficacy against House mice. FGARs should only be used against mice where there is evidence that the local strain is susceptible.
At the workshop in Brussels it was concluded that at this moment, there is not sufficient information and support to restrict FGAR active substances at EU level regarding resistance in mice. The proposed RMM is not relevant for this AR as it concerns a SGAR.

- Provided the other RMMs are applied (pack size, bait stations see below), there is no reason to
restrict the use of SGAR for amateurs, especially in order to control House mice populations, which are the number one problem in the amateur sector.
- Pack size should always be limited for amateur use and SGAR should be sold in smaller amounts than FGARs. A precise computation and list of suggestions is provided. Products intended for use by amateurs should be clearly different from products intended for use by professionals and PCOs.
It is agreed that authorisations for amateurs and professionals can be covered under the same authorisation, but shall be placed on the market as different products (different pack size and separate labelling). The SPC format is already adapted to allow the different uses on one SPC. Looking at the different situations at MS level regarding the use of ARs by the general public MS can still derogate from MR when the refMS has authorised the product for amateurs. RMM on pack sizes is included in 2.3.3.

- Amateurs should have the option to use ARs in and around buildings for the control of rat infestations, since there is evidence that rat infestations almost invariably have an outdoor origin (burrows). Any restriction of an active substance, or a biocidal product, to use 'indoors only' is a de facto restriction preventing use against most rat infestations.
The control of rats in and around buildings for the general public can be approved at the

[4] Available at https://circabc.europa.eu/w/browse/d66ad096-37a1-4903-a3e0-24607ca3f3ea

substance approval stage but it may also be subject to derogation from MR at the product authorisation stage. RMM included in 2.3.2. [May be discussed at WG ENV.]

- Dyes should always be included in the formulations. Using specifically green/blue dyes for ARs which are not absorbed appears as an interesting RMM to monitor both bait uptake (efficacy) and non-target primary exposure.
RMM included in 2.3.2.

- Bittering agents should be included in all bait formulations. Denatonium benzoate at 0.001% (10 mg.kg-1) is currently the most commonly used bittering agent in bait formulations.
RMM included in 2.3.2.

- Baiting area: professionals and trained professionals should conduct surveys prior to application of ARs that consider the extent of the rodent infestation, and the risks posed to humans and non-target species. Information should always be applied on the bait stations but not in the surrounding area.
Survey before baiting should be part of the training for all professionals including farmers. This RMM was agreed on at the workshop in Brussels and WG efficacy. The RMM is included in 2.3.3. No agreed position was reached on the RMM to avoid posting information on baiting areas, this will be left to the MSs to decide at product authorisation.

- For amateur use, tamper-resistant bait stations should always be mandatory, with baits securely fixed inside the bait stations when possible (wax blocks, paste). Loose baits (such as grain and pellets) cannot be excluded, even for amateur use, because of their higher palatability. Using smaller packs and pre-packed bait stations should reduce the risk of accidental human exposure, and possibly pet exposure.
At the workshop in Brussels a large majority agreed that tamper-resistant bait stations with securely fixed baits should always be mandatory for amateur use and that products intended for use by amateurs should be clearly different from products intended for professional use. The bait content of bait stations is to be defined at product authorisation stage as it may depend on rodent species, type of bait, etc. RMM on the use of bait stations for non-professional users is included in 2.3.2 (without mentioning fixation of baits). Harmonisation on the use of loose grains and pellets in sachets for non-professional users seems possible [may be discussed WG TOX].

- For PCOs and professionals, bait can either be presented in tamper-resistant bait stations, or in open trays that are protected from non-target species using a combination of natural cover, materials located on site and materials brought onto site specifically for that purpose. Infestations are likely to be large, and non-target impact will be minimized by optimizing bait presentation to the rodents, and thus minimizing the duration of the treatment. The utility of tamper resistant bait points will vary from site to site and their use should be left to the discretion of the operator, in the light of the risk assessments conducted at the outset of the treatment.
At the workshop in Brussels it was concluded that the use of non-conventional bait stations (e.g. open trays or similar) by trained/certified professionals (PCOs) only should remain possible under certain circumstances. MSs may derogate from MR at the product authorisation stage.RMMs are included in 2.3.2 [may be discussed at WG ENV]

- Pulsed baiting should be used when SGARs are applied to reduce the quantity of bait applied provided data is available to support the efficacy of this practice with particular active substance and biocidal product.
Pulsed baiting is specific for products containing the most potent SGARs only (i.e. flocoumafen, brodifacoum and difethialone) and will be restricted to trained/certified professional users only (PCOs). Efficacy for pulsed baiting needs to be demonstrated and needs to be mentioned specifically on the product SPC/label. Weekly controls are required for pulsed biting. RMM is included in 2.3.2.

- Permanent baiting should not be conducted outdoor unless there is a high risk of re-invasion, because it poses a very high risk to non-target species.

- Permanent baiting may be conducted indoors, particularly where there is a regulatory requirement, or where there is a high risk of re-invasion, because it can be managed to pose a low risk to non-target species.
Permanent baiting indoors and outdoors by trained/certified professionals only should remain possible under certain circumstances. This could be defined in a code of best practice. Permanent baiting for specific locations could be appropriate as part of an IPM strategy based on site specific risk assessments. For outdoor permanent baiting, MSs may derogate from MR at the product authorisation stage. RMM included in 2.3.2 [will be discussed at WG ENV]

- In the first instance, the duration of outdoor baiting should always be limited to 35 days (5 weeks). Subsequent continued rodent activity could indicate that the rodents are resistant to the rodenticide, or that a significant proportion of the infestation are not being treated, and are continually moving into the treated area.
At the workshop in Brussels a large majority agreed, but it was also concluded that in some situations, e.g. sensitive areas or areas subject to constant reinvasion, baiting beyond 35 days will be justified. RMM that products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment is included in 2.3.3.

- Frequency of visits should be left to the discretion of the operator, in the light of the risk assessments conducted at the outset of the treatment. The wide diversity of sites with rodent infestations precludes any strict frequency. However, as a minimum treated sites should be visited once a week.
At the workshop it was concluded that it is preferable that MSs decide to make reference to code of best practices and that frequency of visits is left to the professional. There should be a link between the SPC and the code of best practice which might be difficult for certain MSs which do not yet have such codes available. A general RMM is added to 2.3.3.

- All rodent bodies should be disposed of on each visit by the PCO, and clients should be encouraged to dispose of rodent bodies, taking necessary steps to ensure their safety (providing advice on wearing gloves, minimizing contact, and washing hands after disposal). Specific recommendations for disposal of rodent bodies should be specified (avoid the general sentence "according to local regulations"). For clients and other amateurs, sealing the bodies in two separate plastic bags and safe disposal in the garbage can be considered.
- Uneaten bait should always be removed and disposed of at the end of the treatment. Amateurs may dispose of their remaining uneaten baits by sealing it within two plastic bags and safe disposal in the garbage.
At the workshop in Brussels it was concluded that the RMM 'Removal and disposal of uneaten bait and dead bodies at the end of treatment' can be included at active substance renewal, but the method of disposal and classification of waste will be left to the MSs (e.g. sentence "in accordance with local requirements"). However, the method of disposal should be described specifically on the national SPC and product label. RMM included in 2.3.3.

- Resistance in rodent populations should be managed by ensuring that only effective ARs are used to control population rodents. For House mice, first generation anticoagulants should be avoided unless there is good evidence that populations can be controlled with a particular active ingredient, and for House mice and Norway rats, resistance surveys involving the sequencing of the VKORC1 gene should be conducted for any population of rodents where physiological resistance is suspected. Where mutations of the VKORC1 gene are detected, subsequent use of ARs should be restricted to the active ingredients currently believed to be efficacious against that particular mutation. Such information should be made widely available across all MSs in a format similar to that of the Rodenticide Resistance Action Group (see RRAG, 2010), and should be regularly updated in the light of results generated across all member states.
- In the long term, mapping of the different VKORC1 mutations across all MSs should also be made available online, to allow predictions to be made for new infestations located within areas that have previously been surveyed.
At the workshop in Brussels, a need for a harmonised methodology for monitoring resistance was identified. A first proposal on the set up of a monitoring system taking into account regional information has been received from the expert team. Given the uncertainties about

the protocol to be used, the resources, data collection and sharing, etc. at the time of this renewal, it was decided at WG EFF that appropriate data for resistance monitoring should be provided by the applicants during the next renewal process depending on the feasibility of the implementation of a harmonised resistance monitoring programme at EU level. This has been added as a requirement of further information at 2.3.4.

2.3. Overall conclusions

The outcome of the assessment for flocoumafen in product-type 14 is specified in the BPC opinion following discussions at the 16th meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA website.

2.4. Requirement for further information related to the biocidal product[3]

None identified.

2.5. List of endpoints

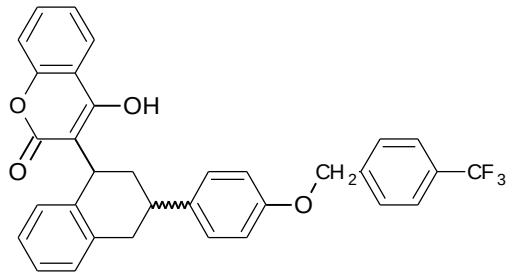
The most important endpoints for the active substance, based on the original evaluation and the revaluation performed for the renewal of approval, are listed in Appendix I.

Appendix I: List of endpoints

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

Active substance (ISO Name)	Flocoumafen *
Product-type	PT14 (Rodenticide)

Identity

Chemical name (IUPAC)	4-hydroxy-3-[(1*RS*,3*RS*;1*RS*,3*RS*)-1,2,3,4-tetrahydro-3-[4-(4-trifluoromethylbenzyloxy)phenyl]-1-naphthyl]coumarin
Chemical name (CA)	4-hydroxy-3-[1,2,3,4-tetrahydro-3-[4-[[4-(trifluoromethyl)phenyl]methoxy]phenyl]-1-naphtalenyl]-2H-1-benzopyran-2-one
CAS No	90035-08-8
EC No	421-960-0 (ELINCS)
Other substance No.	CIPAC No.: 453
Minimum purity of the active substance as manufactured (g/kg or g/l)	Minimum purity 95.5% w/w (50% to 80% cis- and 20% to 50% trans-isomers) *
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None
Molecular formula	$C_{33}H_{25}F_3O_4$
Molecular mass	542.6 g/mol
Structural formula	

** the ISO published common name of flocoumafen should be amended to 50%-80%/20%-50% cis/trans- isomers because the name flocoumafen is currently restricted to 40-60%/60%-40% cis/trans-isomer mixtures.*

Physical and chemical properties

Melting point (state purity)	166.1–168.2 °C (Purity: 99.4 %)
Boiling point (state purity)	Decomposes before boiling (Purity 99.4%)
Thermal stability / Temperature of decomposition	~280 °C
Appearance (state purity)	White, fine crystalline solid (Purity: 99.4 %) TGAI: White, fine crystalline solid (Purity 98.6%)
Relative density (state purity)	1.40 (Purity: 99.4 %)

Surface tension (state temperature and concentration of the test solution)	Not required in view of water solubility < 1 mg/l
Vapour pressure (in Pa, state temperature)	< 1 × 10^{-3} Pa at 20, 25 and 50 °C
Henry's law constant (Pa m^3 mol^{-1})	< 3.871 Pa × m^3/mol
Solubility in water (g/l or mg/l, state temperature)	pH 4: 0.0024 mg/l (T = 20 °C) pH 7: 0.114 mg/l (T = 20 °C) pH 9: 14.0 mg/l (T = 20 °C)
Solubility in organic solvents (in g/l or mg/l, state temperature)	Solvent [g/l; 20°C] Methanol 14.1 Toluene 31.3 n-Octanol 17.4
Stability in organic solvents used in biocidal products including relevant breakdown products	Not relevant
Partition coefficient (log P_{OW}) (state temperature)	pH 4: >6.12 (20°C) pH 7: 6.12 (20°C) pH 9: 5.11 (20°C)
Dissociation constant	pK_a = 4.5
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	ε_{311} = 14162 l × mol^{-1} × cm^{-1} (water, pH 6.8)
Flammability or flash point	Not classified as a flammable solid.
Explosive properties	Not explosive.
Oxidising properties	No oxidizing properties.
Auto-ignition or relative self ignition temperature	No self-ignition of the test substance was observed up to 400 °C. Not self-heating or pyrophoric.

Classification and proposed labelling

with regard to physical hazards	none
with regard to human health hazards	GHS06 GHS08 Repr. 1B; H360D Acute Tox. 1; H300 Acute Tox. 1; H310 Acute Tox. 1; H330 STOT RE 1; H372 (blood)
with regard to environmental hazards	GHS09 Aquatic Acute 1; H400 Aquatic Chronic 1; H410
SCLs and/or M-Factors	Repr. 1B; H360D: C ≥ 0,003% STOT RE 1; H372 (blood): C ≥ 0,05% STOT RE 2; H373 (blood) 0,005%≤ C <0,05% M=10 (acute) M=10 (chronic)

Chapter 2:Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	Dissolution in hexane/dichloromethane/acetic acid 70/30/0.5 (v/v/v). Normal-phase HPLC-UV (235 nm).
Impurities in technical active substance (principle of method)	Dissolution in acetonitrile/dioxane/0.1% phosphoric acid. C18-reversed-phase HPLC-UV (215 nm).

Analytical methods for residues

Soil (principle of method and LOQ)	Extraction with MeOH/water followed by partitioning against n-hexane. Clean-up on NH2 Bond Elut column. C18-reversed-phase HPLC-Fluorescence (Ex = 310 nm, Em = 390 nm). LOQ = 1 µg/kg.
Air (principle of method and LOQ)	Not required.
Water (principle of method and LOQ)	Extraction with hexane. Reversed-phase LC-MS. LOQ = 0.05 µg/L. (Method validated for surface water and groundwater).
Body fluids and tissues (principle of method and LOQ)	Urine: SPE, no further clean-up. Blood: acetontrile extraction, no further clean-up. Liver: extraction with dichloromethane/acetone followed by Bond-Elut CN-U clean-up. Reversed-phase LC-MS, LOQ = 5 µg/L (blood, urine), 5 µg/kg (liver).
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	LC-MS/MS method for the determination of flocoumafen residues in cucumber, wheat, oil seed rape and lemonLOQ = 0.01 mg/kg (all matrices)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	LC-MS/MS method for the determination of flocoumafen residues in meat (beef).LOQ = 0.01 mg/kg

Chapter 3:Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption*:	69-74% at 0.14 mg/kg bw based on radiolabel recovered from urine, tissues (liver, skin and kidneys) and cage wash. 17% at 14 mg/kg bw based on radiolabel recovered from urine, liver and cage wash.
Rate and extent of dermal absorption**:	10% based on physical chemical properties. 4% tier based on comparable molecular mass and log Pow of the other similar second generation anticoagulants
Distribution:	Extensively distributed, with highest tissue levels in liver which is the target organ.
Potential for accumulation:	Yes, half-life of flocoumafen in liver 215 days.

Rate and extent of excretion:	Low dose: 0-35-0.45% in urine and 26.16-23.07% faeces in 7 days High dose: 0.6-6.1% in urine and 63.2-71% in faeces in 72 hours
Toxicologically significant metabolite(s)	None

* at lower doses the oral absorption is expected to be >80%, therefore a correction for oral absorption is not necessary (agreed at TMII2008)
** the dermal absorption value is applicable for the active substance and might not be usable in product authorization

Acute toxicity

Rat LD_{50} oral	0.13-0.5 mg/kg (H300)
Rat LD_{50} dermal	0.43-1.14 mg/kg (H310)
Rat LC_{50} inhalation	0.0006-0.007 mg/l (H330)

Skin corrosion/irritation	Testing not possible due to labelling R27. 1% solution in PEG not skin irritating.
Eye irritation	Non-irritant.
Respiratory tract irritation	Non-irritant.
Skin sensitisation (test method used and result)	Non-sensitizer (Maximisation).
Respiratory sensitisation (test method used and result)	No data

Repeated dose toxicity

Short term

Species / target / critical effect	Rat, increased mean prothrombin and APTT, decreased levels of plasma protein, alkaline phosphatase and cholesterol.
Relevant oral NOAEL / LOAEL	Rat, 28-d, 0.05 mg/kg food (0.0025 mg/kg bw/day) (STOT RE1, H372)

Subchronic

Species / target / critical effect	Rat, prothrombin time prolongation and haemorrhaging.
Relevant oral NOAEL / LOAEL	Rat, 90-d, 0.05 mg/kg food (0.0025 mg/kg bw/day) (STOT RE1, H372)
Relevant dermal NOAEL / LOAEL	No data available, no data required (STOT RE1, H372).
Relevant inhalation NOAEL / LOAEL	No data available, no data required (STOT RE1, H372).

Genotoxicity	No genotoxic potential, in *in vitro* and *in vivo* genotoxicity studies.

Carcinogenicity

Species/type of tumour	No data available, no data required.
Relevant NOAEL/LOAEL	No data available, no data required.

Reproductive toxicity

Developmental toxicity

Species/ Developmental target / critical effect	Rabbits, abortion due to bleeding. No developmental or teratogenic effects in animal studies. Classification with H360D based on read-across from warfarin
Relevant maternal NOAEL	NOAEL maternal toxicity in rabbit 0.002 mg/kg bw/day NOAEL maternal toxicity in rat 0.02 mg/kg bw/day
Relevant developmental NOAEL	>0.004 mg/kg bw/day in rabbit

Fertility

Species/critical effect	No data available, no data required.
Relevant parental NOAEL	No data available, no data required.
Relevant offspring NOAEL	No data available, no data required.
Relevant fertility NOAEL	No data available, no data required.

Neurotoxicity

Species/ target/critical effect	No data available, no data required.

Developmental Neurotoxicity

Species/ target/critical effect	No data available, no data required.

Immunotoxicity

Species/ target/critical effect	No data available, no data required.

Developmental Immunotoxicity

Species/ target/critical effect	No data available, no data required.

Other toxicological studies

No data available, no data required.

Medical data

No evidence of toxicological concern from medical surveillance of manufacturing plant personnel

Summary

	Value	Study	Safety factor
$AEL_{long\text{-}term}$	$8.3*10^{-6}$ mg/kg bw/day (chronic)	90-days, rat	300
$AEL_{medium\text{-}term}$	$8.3*10^{-6}$ mg/kg bw/day (medium)	28-days, rat	300
$AEL_{short\text{-}term}$	$6.7*10^{-6}$ mg/kg bw/day (acute)	Teratogenicity study, rabbits	300
ADI[5]	Not allocated, not necessary.		
ARfD	Not applicable		

MRLs

Relevant commodities	Product is not intended to come into contact with food or feeding stuffs, contamination of food and feeding stuff can be excluded.

Reference value for groundwater

According to BPR Annex VI, point 68	0.1 µg/L

Dermal absorption

Study (*in vitro/vivo*), species tested	-
Formulation (formulation type and including concentration(s) tested, vehicle)	-
Dermal absorption values used in risk assessment	10% based on phys-chem properties 4% based on comparable molecular mass and log Pow of other similar second generation anticoagulantia

Acceptable exposure scenarios (including method of calculation) [6]

Formulation of biocidal product	-

[5] If residues in food or feed.

[6] At product authorisation new human exposure calculations should be performed taking into account HEEG opinion 10 and 12.

Intended uses	Storm BB is a rodenticide product in form of a ready-to-use wax block bait with a mass of 20 g, based on wheat grain containing 0.005% of the active substance For the control of mice and rats in and around buildings
Industrial users	-
Professional users	Trained professionals Exposure scenario: Application + post application - Placing wax bait in rodent burrows and loading of bait stations with wax bait - Collection of uneaten bait, empty packages and dead animals, disposed of as controlled waste Frequency of daily use: - Loading and placement: The dermal exposure is based on the dislodgeable residue per wax block for securing wax blocks in bait stations for 74.9 exposure events per day - Clean-up: The dermal exposure is based on the dislodgeable residue per wax block for clean-up and disposal for 74.9 exposure events (based on EBRC Report). the risk index (exposure/AELmedium or long-term) is 0.6 including the use of gloves. Non-trained professionals Exposure scenario: Application + post application - Placing wax bait in rodent burrows and loading of bait stations with wax bait - Collection of uneaten bait, empty packages and dead animals, disposed of as controlled waste Frequency of daily use: - Loading and placement: 2 campaigns per year (assuming treatments to be seasonal), 3 to 4 bait placing periods per campaign, 10 bait points per farm, 3 wax blocks per bait point. For the dermal exposure the value of 30 wax blocks handled per day is used. - Clean-up: The dermal exposure is based on the dislodgeable residue per wax block for clean-up and disposal of 30 wax blocks. For the products used on a repetitive or daily basis, the risk index (exposure/AELmedium or long-term) is 0.6, without gloves

Non-professional users	Exposure scenario: Application + post application - Placing wax bait in rodent burrows and loading of bait stations with wax bait Collection of uneaten bait, empty packages and dead animals, disposed of as controlled waste Frequency of daily use: - Loading and placement: 2-4 campaigns per year, 3 to 4 bait placing periods per campaign , 2 bait points per location, 3 max blocks per bait point. For the dermal exposure the value of 6 wax blocks handled per day is used. - Clean-up: The dermal exposure is based on the dislodgeable residue per wax block for clean-up and disposal of 6 wax blocks. For products used on a single occasion, the risk index (exposure/AELmedium or long-term) is 0.17, without gloves
General public	Infants ingesting 10 mg or 5 g of wax block material. Systemic Exposure = 3.8 x 10^{-5} mg/kg/d (Infants ingesting 10 mg), 1.9 x 10^{-2} mg/kg/d (Infants ingesting 5g).
Exposure via residue in food	Not applicable

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	DT50 > 1 yr (estimate based on 5-day study at T = 50 °C)
pH 7	DT50 > 1 yr (estimate based on 5-day study at T = 50 °C)
pH 9	DT50 > 1 yr (estimate based on 5-day study at T = 50 °C)
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	active substance: t½E = 1.67 d ("normal" value in April) • 4-(Trifluoromethyl)-benzoic acid (CAS-No. 455-24-3) • 4-hydroxy-3-[3-(4-hydroxyphenyl)-1,2,3,4-tetrahydro-1-naphthyl]coumarin (no CAS-No. allocated) • Plus two unidentified transformation products

Readily biodegradable (yes/no)	No
Biodegradation in seawater	Not required
Non-extractable residues	Not required
Distribution in water / sediment systems (active substance)	Not required
Distribution in water / sediment systems (metabolites)	Not required

Route and rate of degradation in soil

Mineralization (aerobic)	No reliable mineralization rate can be determined. CO2- formation was max. 15.6%, day 70; and 13.4%, end of study (day 120); determined for trifluoromethylphenyl labelled 14C-flocoumafen
Laboratory studies (range or median, with number of measurements, with regression coefficient)	Geometric mean DT50 = 213 days (range 71-442 days (n=4, 20°C), 4 soils using two labelling positions) Geometric mean DT50 = 404 days at 12°C
Field studies (state location, range or median with number of measurements)	No reliable data available.
Anaerobic degradation	No degradation under anaerobic conditions
Soil photolysis	Not required
Non-extractable residues	Non-extractable residues: max. 47.4% end of study (120 days)
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	The sum of metabolites never exceeded 3.7% for both labels at any sampling date.
Soil accumulation and plateau concentration	No data available

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	Koc = 68510 (cis-isomer) (HPLC method) Koc = 134858 (trans-isomer) (HPLC method) Koc = 101684 (mean) (HPLC method) No

Fate and behaviour in air

Direct photolysis in air	No data available
Quantum yield of direct photolysis	No data available

Photo-oxidative degradation in air	QSAR estimation: t½ (Ozone) = 2.015 h t½ (OH) = 1.479 h
Volatilization	Not expected; p < 10^{-3} Pa; H < 3.871 Pa × m^3/mol (QSAR estimation: 7.43 x 10^{-8} Pa x m^3/mol)

Reference value for groundwater

According to BPR Annex VI, point 68	0.1 µg/L

Monitoring data, if available

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

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 h	Mortality, LC50	0.07 mg/L
Invertebrates			
Daphnia magna	48 h	Immobility, EC50	0.18 mg/L
Algae			
Pseudokirchneriella subcapitata	72 h	Growth inhibition	EbC50 & ErC50 >18.2 mg/L NOEbC 1.7 mg/L NOErC ³18.2 mg/L
Microorganisms			
Mixed species activated sludge	3 h	Respiration inhibition	EC50 > 4.0 mg/L NOEC 4.0 mg/L

Effects on earthworms or other soil non-target organisms

Acute toxicity to earthworms	EC_{50} > 1000 mg/kg dry soil or 882.4 mg/kg wet soil
Reproductive toxicity to ……	No data available
Toxicity to plants	EC_{50} ≥ 714 mg/kg dry soil or 630.0 mg/kg wet soil

	NOEC = 179 mg/kg dry soil or 157.9 mg/kg wet soil

Effects on soil micro-organisms

Nitrogen mineralization	EC_{10} 12.1 mg/kg dry soil or 10.7 mg/kg wet soil EC_{50} > 1000 mg/kg dry soil or 882.4 mg/kg wet soil
Carbon mineralization	NOEC > 1000 mg/kg dry soil or 882.4 mg/kg wet soil EC_{50} > 1000 mg/kg dry soil or 882.4 mg/kg wet soil

Effects on terrestrial vertebrates

Acute toxicity to mammals	LD50 = 0.13 mg/kg bw (oral single dosage, rat) Acute toxicity
Acute toxicity to birds	LD50 = 24 mg/kg bw (oral single dosage, *Anas platyrhynchos*)
Dietary toxicity to birds	5-day dietary toxicity (*Anas platyrhynchos*): LC50 = 12 mg/kg diet ⇔5.6 mg/kg bw/day
Reproductive toxicity to birds	20 wks reproduction toxicity (*Coturnix japonica*): NOEC>0.063 mg a.i./kg diet, ⇔ NOEL>0.0075 mg a.i./kg bw/d, derived by read-across from a reproductive toxicity study with difenacoum

Effects on honeybees

Acute oral toxicity	Not required
Acute contact toxicity	Not required

Effects on other beneficial arthropods

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

Bioconcentration

Bioconcentration factor (BCF)	BCF_{fish} (kinetic) = 24,300 L/kg wwt BCF = 15,820 kg/kg wwt (earthworms) (Estimate based on log Pow = 6.12)
Depuration time (DT_{50})	No data available
Depuration time (DT_{90})	No data available

Level of metabolites (%) in organisms accounting for > 10 % of residues	Not required

Chapter 6: Other End Points

None

Appendix II: List of studies submitted for the renewal of approval process

Data protection is claimed by the applicant in accordance with Article 60 of Regulation (EU) No 528/2012.

Section No / Reference No[7]	Author(s)[8]	Year	Title[9] Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/ No)	Owner
II-9.1.4/01	[redacted]	2011	Fish, bioconcentration of Flocoumafen according to the OECD-Guideline 305 and EU method C.13 Fraunhofer Institute for Molecular Biology and Applied Ecology, Schmallenberg, Germany, Report no. EBR-003/4-10 BASF ID: 2010/1178749 GLP / unpublished	Yes	BASF
II-9.2.1/01	[redacted]	2007	Soil microorganisms: Effects of Flocoumafen on nitrogen and carbon transformation Fraunhofer Institute for Molecular Biology and Applied Ecology, Schmallenberg, Germany, Report no. EBR-003/3-35 BASF ID: 2007/1022271 GLP / unpublished	Yes	BASF
II-9.2.2/01	[redacted]	2007	Earthworm acute toxicity test: acute toxicity of Flocoumafen on *Eisenia fetida* Fraunhofer Institute for Molecular Biology and Applied Ecology,	Yes	BASF

[7] ***Section Number/Reference Number*** should refer to the section number in Doc III-A or III-B. If the study is non-key, and hence not summarised in Doc III but mentioned in Doc II, it should be included in the reference list alongside related references and its location in Doc II indicated in brackets. (If there is a need to include a cross-reference to PPP references then an additional column can be inserted).

[8] ***Author's Name*** should include the author's surname before initial (s) to enable the column to be sorted alphabetically. If the Human Rights Charter prevents author's surnames on unpublished references being included in non-confidential documents, then it will be necessary to consider including 'Unpublished [number/year & letter] ' in Doc II, and both ' Unpublished [number/year & letter]' and the 'Authors Name' in the reference list'. This may necessitate the need for an additional column to state whether a reference is unpublished which can then be sorted.

[9] ***Title, Source (where different from company), Company, Report No., GLP (where relevant), (Un)Published*** should contain information relevant to each item (ideally on separate lines within the table cell for clarity). If useful, the name of the electronic file containing the specific study/reference could be added in brackets.

Section No / Reference No[7]	Author(s)[8]	Year	Title[9] Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/ No)	Owner
			Schmallenberg, Germany, Report no. EBR-003/3-08 BASF ID: 2007/1028165 GLP / unpublished		
II-9.2.3/01	[redacted]	2007	Terrestrial plants, growth test: Effect of Flocoumafen on the seedling emergence and growth of *Avena sativa*, *Lactuca sativa*, *Phaseolus aureus*, *Raphanus sativus*, *Sinapis alba*, and *Triticum aestivum* Fraunhofer Institute for Molecular Biology and Applied Ecology, Schmallenberg, Germany, Report no. EBR-003/4-40 BASF ID: 2007/1033910 GLP / unpublished	Yes	BASF
II-9.7/01	[redacted]	2012	Bioaccumulation in terrestrial oligochaetes - Uptake and elimination of flocoumafen (BAS 322 I) in *Eisenia fetida* Fraunhofer Institute (IME), Schmallenberg, Germany Report no. EBR-003/3-25, BASF ID: 2011/1284061 GLP / Unpublished	Yes	BASF