Vitenskapskomiteen for mattrygghet
Norwegian Scientific Committee for Food Safety

Risk assessment of the fungicide Infinito with the active substances fluopicolide and propamocarb-HCL

Opinion of the Panel on plant protection products of the Norwegian Scientific Committee for Food Safety

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Summary

Infinito is a new fungicide containing the two active substances fluopicolide and propamocarb-HCL. Infinito is a new generation fungicide to protect potatoes against the blight pathogen *phytophtora infestans.* The risk assessment was finalized at a meeting Mai 29, 2012, by the Panel on plant protection products of the Norwegian Scientific Committee for Food Safety (VKM).

The Norwegian Food Safety Authority would like, in this regard, an assessment of the following:

- The fate and behaviour in the environment and the ecotoxicological effects and risks with regard to the properties of Infinito and the active substances. The Panel is particularly asked to look at the following:
    - The persistence of fluopicolide and its metabolites.
    - The leaching potential of fluopicolide and its metabolites.

VKM considers both fluopicolide and its main metabolite M-01 (2,6-dichlorobenzamid (BAM)) to be persistent in Norwegian soils and surface waters.

Other conclusions from VKM are as follows:

- Fluopicolide and its main metabolite may have a significant potential for soil accumulation after repeated use under Norwegian conditions.
- Fluopicolide shows low mobility in both studies and modelling. Metabolite M-01 (BAM) is however highly mobile.
- There is minimal risk for toxic effects of fluopicolide to terrestrial and aquatic organisms with the proposed application regime.

Background

The Panel on plant protection products of the Norwegian Scientific Committee for Food Safety (VKM) performs risk assessments in the context of pesticide registration cf. Regulation on Pesticides § 4. The Norwegian Food Safety Authority, National Registration Section, is responsible for reviewing and evaluating the documentation submitted by the pesticide notifier. The Norwegian Food Safety Authority takes the final regulatory action regarding registration or deregistration of pesticides based on VKMs risk assessment, along with a comparative assessment of risk and benefits and the availability of alternatives (the principle of substitution).

The Norwegian Food Safety Authority submitted a request on April 20, 2012 for VKM to perform a risk assessment on use of the pesticide Infinito containing the active substances fluopicolide and propamocarb-HCL. The environmental risk assessments of the product were finalized by VKM in June, 2012.

Terms of reference

Infinito is a new fungicide containing the active substances fluopicolide and propamocarb-HCl. Fluopicolide is a new active substance in Norway, but propamocarb-HCl is already approved in several products. Infinito is a new-generation fungicide to protect potatoes against the blight pathogen *Phytophthora infestans*.

The Norwegian Food Safety Authority would like, in this regard, an assessment of the following:

- The fate and behaviour in the environment and the ecotoxicological effects and risks with regard to the properties of Infinito and the active substances. The Panel is particularly asked to look at the following:
    - The persistence of fluopicolide and its metabolites.
    - The leaching potential of fluopicolide and its metabolites.

1 Background documentation

VKM's risk assessment is based on the Norwegian Food Safety Authority's evaluation (2012) of the documentation submitted by the applicant. The Norwegian Food Safety Authority publishes both their evaluation of Infinito and their final regulatory action on the registration of the pesticide product at their homepage www.mattilsynet.no

2 Procedure

The first three steps of the risk assessment (hazard identification, hazard characterization and assessment of exposure) are performed by the Norwegian Food Safety Authority and involve an assessment of the documentation submitted by the pesticide notifier. The resulting report on hazard identification, hazard characterization and assessment of exposure, from which the summary is included in the present document, is then reviewed by VKM. This review may result in some amendments in the original documents of both the summary and the full report issued by the Norwegian Food Safety Authority (2012). The fourth step (risk characterization) is based on the three first steps and is VKM's conclusions or risk assessment.

2.1 Environmental risk assessment

The environmental risk assessment of pesticides involves predictions of exposure concentrations in various environmental compartments (e.g. soil and surface waters) that may occur after application of the pesticide. These predicted effect concentrations (PECs) are compared to exposure levels that are known to cause toxic effects to important groups of organisms representing the environmental compartments.

The environmental fate and possible ecotoxicological effects of pesticides are investigated in several laboratory- and field experiments. In environmental risk assessments of pesticides, Predicted Environmental Concentrations (PECs) are estimated by use of different scenarios for different parts of the environment (terrestrial, aquatic). The first parameter estimated is usually the initial concentration (PIEC, Predicted Initial Environmental Concentration), e.g. the concentration just after application (usually spraying). PIEC in soil is calculated assuming a homogenous distribution of areal dose in the upper 5 cm soil layer. For surface water, the PIEC is based on deposition of pesticides from spray drift in a standard size water body. The calculations are performed with application of buffer zones between the sprayed area and the water body.

The further exposure regime in different compartments is affected on the fate of the pesticide. The fate is dependent on processes such as photodegradation, hydrolysis, biodegradation and sorption to soil particles. These processes are studied in several standardised laboratory tests. In addition, field tests are used to study the dissipation of the pesticide in various agricultural soils. Based on the experimental fate studies, factors describing different fate processes may be derived and used in models that describe the fate of the pesticide in the soil as well as the transport to surface water and ground water. The concentrations of the pesticide in water are estimated by use of models with relevant scenarios based on EU's FOCUS-scenarios. The models produce maximum PEC and average PEC calculated for specified periods after pesticide application. In the surface water scenarios PEC is also calculated for the sediment phase.

Then the Toxicity Exposure Ratio (TER) is estimated for different groups of organisms. The TER is calculated as the ratio between the toxicity for the organism in question (expressed as

LC50, EC50, NOEC etc., depending on organism and study type) and PEC or PIEC. Trigger values for TER, which express the acceptability of the risk for different organisms, have been defined by the EU. The risk is considered minimal when the TER does not exceed the trigger value.

In the terrestrial environment, the risk for toxic effects on bees and non-target arthropods is assessed according to other criteria. Hazard quotients for oral- (HQ_O) and contact toxicity (HQ_C) are estimated for bees. HQ_O evt. HQ_C is the ratio between the standardized area dose of the product (g v.s./ha) and acute toxicity for the bee (LD50, µg active ingredient/bee). Field experiments and expert evaluation is triggered whenever the hazard quotient is above 50.

For the non-target arthropods, the estimated hazard quotient (HQ) is the ratio between the area dose of the product (g active ingredient/ha), which is multiplied with a factor for multiple applications (MAF, multiple application factor) when appropriate, and the acute toxicity for the organism (LR50, g active ingredient/ha). According to EU, whenever the ratio value exceeds 2, further investigations are triggered.

VKM makes use of a scale in order to describe the risk of exposure for different organisms which live within and outside the spraying field. The scale is based on the ratio between the estimated exposure and the limit or the ratio between the TER and the TER trigger value designated each group of organism.

The following risk scale is used:

Very high risk	more than 500% of the limit
High risk	300 – 500% of the limit
Medium risk	150-300% of the limit
Moderate risk	110-150% of the limit
Minimal risk	the limit is not exceeded

The estimates of exposure concentrations are based on maximal concentrations, which exist during or shortly after spraying. The group of organism assessed (for example birds or leaf dwelling non-target organisms) is not always present during the period of maximal concentration. In the final risk assessment, VKM therefore takes into consideration whether, or to which extent, the organism in question actually will be exposed. This may cause that the risk is assessed lower than indicated by the scale above.

Additionally, uncertainties in the data base both with regard to establishments of limits and models of exposure concentrations are taken into consideration if relevant. This may also cause that the risk is assessed lower or higher than the risk scale. Any deviation from the risk scale is justified in this document.

3 Summary by the Norwegian Food Safety Authority (Hazard identification, hazard characterization and exposure assessment)

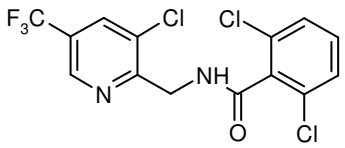
Infinito is a new product containing propamocarb-HCl (625 g/L) and the new active ingredient fluopicolide (62.5 g/L). The product is a suspension concentrate (SC) formulation.

Infinito is a new-generation fungicide to protect potatoes against the blight pathogen *Phytophthora infestans.* Fluopicolide represent a new chemical class, acylpicolides, which works by disorganizing the pathogen's cell structure and propamocarb-HCl which is a well know and established active ingredient and works with systemic behaviour.

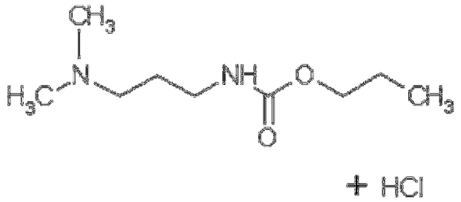
The proposed application rate is from 1.2 L product (750 g propamokarb-HCl and 75 g fluopicolide) to 1.6 L product (1000 g propamokarb-HCl and 100 g fluopicolide) per hectare. The product should be applied in a volume of 150–400 L water per hectare with a broadcast sprayer. Maximum four applications per year using the lowest dose and three applications when using the maximum dose. The application interval is 7–10 days, and no later than 7 days before harvest.

Both active ingredients are evaluated in the EU and included in Annex I.

3.1 Identity and physical/chemical data

Product name	Infinito
Formulation	Suspension concentrate
Active substance	Fluopicolide
Concentration of active substance	62.5 g/L
IUPAC-name	2,6-dichloro-N-[3-chloro-5-(trifluoromethyl)-2-pyridylmethyl]benzamide
CAS number	239110-15-7
Structural formula	

Molecular weight		383.6 g/mole
Water solubility	Moderate	2.9 mg/L (20°C)
Vapour pressure	Low	3.03 x 10^{-7} Pa (20°C)
Henrys law const.	Low	4.15 x 10^{-5} Pa m^3/mole
log Pow	Medium	2.9 (20°C)

pKa	No dissociation
Active substance	Propamocarb-HCl
Concentration of active substance	625 g/L
IUPAC-name	Propyl 3-(dimethylamino) propylcarbamate hydrochloride
CAS number	25606-41-1 (Propamocarb HCl), 24579-73-5 (Propamocarb)
Structural formula	

Molecular weight		224.7 g/mole
Water solubility	Moderate	2.9 mg/l (20°C)
Vapour pressure	Medium	1.66 x 10^{-3} Pa (20°C)
Henrys law const.	Low	8.5 x 10^{-9} Pa m^3/mole
log Pow	Low	-1.3 (20°C)
pKa		9.6 (20°C)

3.2 Mammalian toxicology

Mammalian toxicology is not discussed in this report.

3.3 Environmental fate and ecotoxicological effects

This assessment is based on an Estonian product evaluation for the Northern zone in the EU (E1). This is in turn based on documentation and a Draft Registration Report submitted by the applicant as well as Draft Assessment Reports for the active substances fluopicolide (UK 2005) and propamocarb (Ireland 2004).

3.3.1 Environmental fate and behaviour

3.3.1.1 *Degradation in soil*

Fluopicolide is initially degraded in soil to form the hydroxylated metabolite M-03, and then undergoes cleavage to form M-02 containing the pyridine ring and M-01 containing the phenyl ring. Metabolite M-01 (2,6-Dichlorobenzamide, BAM) is a well-known metabolite also from the active substance dichlobenil. Un-extracted soil bound residues account for

between 5 and 23% of the applied fluopicolide at the end of the soil laboratory studies. Levels of carbon dioxide were low, with less than 3% of the applied radioactivity by the end of the study. The metabolites M-01, M-02 and M-03 were observed in aerobic soil laboratory degradation studies conducted with the parent. M-01 and M-03 can be defined as major metabolites exceeding 10% of applied radioactivity. M-01 has been identified in soils with maximum percentages ranging from 5 to 40%. The occurrence of M-03 has been shown to have a strong pH dependence and the metabolite was only observed as a major metabolite in acidic soils (<pH 6) at a maximum of 11%, whilst in neutral to alkali soils it was either not detected or detected occasionally at a maximum of 3%. M-02 was detected as a minor metabolite in soil at a maximum of 7% under aerobic conditions before declining to less than 2%.

An overview over fluopicolide's metabolites and where they are observed are given in the Draft Registration Report (E1, Section 5, Table 9-2, page 11/137).

Fluopicolide showed low to moderate degradation rates in aerobic soil (DT50: 194-333 days, geomean: 271 days), and low degradation rates (to M-01 and M-02) in anaerobic soil (DT50: 424 days). M-03 was rapidly degraded (DT50: 0.1-4.7 days) in soil (to M-01 and M-02) under aerobic conditions. It was not possible to derive reliable degradation rates for M-01 in studies conducted with the parent or M-03. Supplemental data were provided by a laboratory study conducted with the metabolite M-01 incubated under EPA conditions for up to 365 days (DT50: 808-1848 days). M-02 was very rapidly degraded in soil to a number of metabolites (DT50: 2.5-3.0 days), with a significant portion (>20%) completely mineralised to CO_2.

The potential for accumulation of fluopicolide and its metabolites has been investigated over a four year period at Senas (Southern France), Philippsburg (Germany) and Appilly (Northern France). The study design at all sites represented a worst-case assessment with a single annual application of 400 or 500 g a.s./ha each year to bare soil. EFSA concluded that fluopicolide residues had reached plateau concentrations in the Philippsburg and Senas trials (high: 0.34-0.39 mg/kg, low: 0.082-0.094 mg/kg), but the results were inconclusive in the Appilly trial. For M-01 residues remaining were lower and appeared to reach a plateau only in the Senas trial (high: 0.047 mg/kg, low: 0.015 mg/kg). The metabolites M-02 and M-03 were rapidly degraded in soil and were either not detected or disappeared completely within one month.

Soil dissipation studies were conducted at six European locations to investigate the behaviour of fluopicolide and its soil metabolites M-01, M-02 and M-03 under field conditions. Generally M-02 and M-03 were rapidly degraded in soil and detected only in a few early time points at levels close to the limit of quantification. The experimental data were evaluated to determine degradation half-lives (normalised to 20 °C) for fluopicolide (geomean DT50: 134 days), its metabolite M-01 (geomean DT50: 53 days) and at one site for the metabolite M-03 (worst-case DT50: 37 days). Under field conditions, the dissipation behaviour of fluopicolide was found to be biphasic, with rapid initial degradation followed by a slower second phase of dissipation.

Propamocarb-HCl was metabolised under aerobic conditions in top soils (DT50: 11-137 days) to the principal products carbon dioxide (60 to 90%) and non-extractable soil bound residues (maximum 10 to 34%). Several unidentified metabolites were detected although none exceeded 5.5% of applied radioactivity.

The route of metabolism of propamocarb-HCl under anaerobic conditions follows basically the same route as the metabolism under aerobic conditions although it is slower (DT50: 66-459 days). No significant degradation products were formed under anaerobic conditions. Field

dissipation studies for propamocarb-HCl were conducted at two locations in the USA (DT50: 17-24 days).

3.3.1.2 *Sorption/mobility*

Fluopicolide showed low to medium mobility (Koc: 321). The metabolites showed higher mobility: M-01 (Koc: 41), M-02 (Koc: 6.0), M-03 (Koc: 109), M-05 (Koc: 26) and M-10 (Koc: 6.3). All values are arithmetic means.

A lysimeter study was conducted in Germany in an acidic silty sand soil with low organic carbon content over a three year period with lysimeters treated at the maximum annual application rate (400 g/ha) in the first year and one lysimeter re-treated in the second year. The study suggested that there is low potential for fluopicolide and the metabolites M-02 and M-03 to appear in groundwater even under unfavourable soil and weather conditions. It was not possible to detect M-01, since the radiolabelling was in the pyridine ring. A number of metabolites (M-05, M-10, M-11, M-12, M-13, M-14, M-15 and M-16) were detected in concentrations ranging from 0.080 to 0.902 µg/L in the leachate. EFSA have concluded that all the fluopicolide metabolites are considered not relevant according to the guidance document on groundwater metabolites.

Propamocarb-HCl showed moderate potential for mobility (Koc: 536).

3.3.1.3 *Degradation in water*

Fluopicolide and the metabolite M-01 were stable to hydrolysis and photolysis under abiotic conditions. The rate of hydrolysis of M-03 was strongly dependent on pH (DT50: 8.4 minutes, 45 minutes, 4.7 hours and 46 hours at pH 8, 7, 6 and 5, respectively).

In water/sediment systems fluopicolide was relatively stable and dissipated in the water by a combination of degradation and partitioning to sediment. Fluopicolide undergoes cleavage to form the metabolites M-02 and M-01. M-01 was detected as a major metabolite (max 18.2%) in the water phase of aerobic water sediment systems and was also observed as a minor metabolite in the sediment phase. No other major metabolites (>10 %) were detected. M-02 was detected as a minor metabolite in the water phase (max 7.4%) and was observed at detectable levels in the sediment (<1%).

Rapid dissipation of fluopicolide from the water phase was observed in sediment with high organic carbon content and cation exchange capacity. Fluopicolide showed similar degradation rates in abiotic and biotic water sediment systems, indicating that the degradation was not enhanced by microbial activity in water (DT50 (water dissipation): 8.9-263 days, DT50 (total system): 873-1428 days.)

Propamocarb-HCl was stable to hydrolysis and photolysis under abiotic conditions.

Propamocarb-HCl was readily degraded (DT50: 10-15 days) in both aerobic and anaerobic water sediment systems, with up to 37% observed in the aerobic sediment phase. Overall DT50 values for degradation in water sediment systems were 16 to 21 days. The compound was readily mineralised to carbon dioxide with no accumulation of intermediate degradation products. Sediment bound residues represented <10% after 105 days.

3.3.1.4 *Fate in air*

Fluopicolide has a very low vapour pressure and Henry's Law constant and thus would not be expected to be found in any significant concentration in the air. The theoretical half-life is 2.2 to 3.4 days.

Propamocarb-HCl also has a very low vapour pressure and Henry's Law constant and would not be expected to be found in any significant concentration in the air. The theoretical half-life is <0.17 days.

3.3.2 ENVIRONMENTAL EXPOSURE

3.3.2.1 *Soil*

The highest PEC_{soil} values arise from the EU FOCUS-scenario for onions (3 x 100 g fluopicolide/ha and 3 x 1000 g propamocarb-HCl/ha with 10%, 10% and 25% crop interception, interval 7 days). This is the same application scheme as for potatoes in Norway, but with lower crop interception, i.e. more worst case. Using the Finnish PEC_{soil}-calculator, the rapporteur member state (RMS) gives the following values for fluopicolide, its metabolites and for propamocarb-HCl (which is rapidly degraded to carbon dioxide and non-extractable soil bound residues with no significant metabolites formed):

Fluopicolide	PEC_{soil}, max = 0.79 mg/kg, initial = 0.33 mg/kg
M-01	PEC_{soil}, max = 0.0480 mg/kg
M-02	PEC_{soil}, max = 0.0260 mg/kg
M-03	PEC_{soil}, max = 0.0298 mg/kg
Propamocarb-HCl	PEC_{soil}, max = 8.99 mg/kg, initial = 3.33 mg/kg

3.3.2.2 *Groundwater*

The predicted 80th percentile average groundwater concentrations in potatoes (BBCH 21-95) at 1 m depth (4x100 g fluopicolide/ha, 4x1000 g propamocarb-HCl/ha, 50%, 80%, 80% and 50% interception, 7 d interval, every year, FOCUS PEARL and PELMO) are used. This is earlier application and one more application per season than the Norwegian GAP (BBCH 40-89, 3 applications).

Concentrations of **fluopicolide**, metabolite M-02 and the lysimeter metabolite M-14 were predicted to be <0.1 µg/L for both the Hamburg and Jokioinen scenarios. The metabolites M-01 (max 2.786 µg/L), M-03 (max 0.302 µg/L) and several lysimeter metabolites (M-05 max 0.913 µg/L, M-10 max 0.806 µg/L and M-11 max 0.624 µg/L, M-12 max 0.416 µg/L, M-13 max 0.353 µg/L) were predicted to reach groundwater at concentrations in excess of 0.1 µg/L.

Propamocarb-HCl concentrations were predicted to be ≤0.01 µg/L in all of the FOCUS scenarios, except for Jokioinen (maximum value: 0.195 µg/L). The predicted concentrations at Jokioinen with the PEARL model are a factor of 50 to 100 times higher than those predicted with the PELMO model, whilst all other scenarios are consistent. Thus the PEARL values at Jokioinen are considered to be outliers. Since propamocarb-HCl is readily mineralised to carbon dioxide with no accumulation of intermediate degradation products, no modelling of metabolites is considered necessary.

3.3.2.3 *Surface water*

PEC values have been calculated for the use of in potatoes (4x100 g fluopicolide/ha, 4x1000 g propamocarb-HCl/ha with 50% interception, which is one more application than the Norwegian GAP).

The maximum PECsw values for **fluopicolide** were 97.0, 10.6 and 1.38 µg a.s./L for Step 1, 2 and 3, respectively. The corresponding sediment values were 308, 33.3 and 7.84 µg a.s./kg. The maximum Step 2 PECsw values were 1.49, 0.35 and 0.39 µg/L for the metabolites M-01, M-02 and M-03, respectively. The corresponding sediment values were 0.61, 0.02 and 0.42 µg/kg.

The maximum PECsw values for **propamocarb-HCl** were 811 and 45 µg a.s./L for Step 1 and 2, respectively. The corresponding sediment values were 4190 and 228 µg a.s./kg. Since propamocarb-HCl is readily mineralised to carbon dioxide with no accumulation of intermediate degradation products, no modelling of metabolites is considered necessary.

3.3.3 EFFECTS ON TERRESTRIAL ORGANISMS

For mammals and birds, the risk assessment is performed according to the EU Guidance Document for Birds and Mammals (EFSA 2009). The EU triggers (birds and mammals) are $\geq$10 and $\geq$5 for TER_{acute} (TER_a) and $TER_{long\text{-}term}$ (TER_{lt}), respectively.

3.3.3.1 *Mammals*

Fluopicolide showed low acute toxicity (LD50: >5000 mg a.s./kg bw). In a chronic toxicity test, the NO(A)EL was 20 mg a.s./kg bw/d. Metabolite M-01 showed moderate acute toxicity (LD50: 500 mg/kg bw). The metabolites M-02, M-05 and M-10 showed low acute toxicity (LD50: >2000, >5000 and >5000 mg/kg bw, respectively).

Fluopicolide pass the EU trigger value for acute exposure (TER_a >235) according to the EU screening step with an application rate of 4x100 g a.s./ha in potatoes. Fluopicolide also passes the EU trigger for chronic exposure (TER_{lt} 7.9) calculated according to the EU Tier 1 scenarios.

Propamocarb-HCl showed moderate acute toxicity (LD50: >1330 mg a.s./kg bw). In a chronic toxicity test, the NO(A)EL was 104 mg/kg bw/d.

According to Tier 1 calculations using an application rate of 1000 g a.s./ha in potatoes, propamocarb-HCl pass the acute and long-term trigger for most of the scenarios (TER_a 21, TER_{lt} 4.1). The failure to meet the acceptability trigger for small herbivorous mammals (vole) do not trigger higher tier studies, since other mammal scenarios give acceptable risk.

Infinito showed low acute toxicity (LD50: >2000 mg/kg bw). A comparison of the acute LD50 values derived for the formulation and the active substances indicates that the formulation is not more toxic than expected based on the content of of the active ingredient. Thus, the risk assessment performed above covers the risk from use of Infinito.

3.3.3.2 *Birds*

Fluopicolide showed low acute toxicity (LD50: >2250 mg a.s./kg bw) and low short-term dietary toxicity (LC50: >5620 mg a.s./kg diet, LDD50: >1744 mg a.s./kg bw/d). In a chronic toxicity test, the NOEC was 1000 mg a.s./kg diet (NOEL: 89 mg a.s./kg bw/d). Metabolite M-01 showed moderate short-term dietary toxicity (LC50: 3897 mg/kg diet, LDD50: 1171 mg/kg bw/d).

Fluopicolide pass the EU trigger values for acute (≥10) and long-term (≥5) exposure (TER_a >79, TER_{lt} 12) according to the EU screening step with a application rate of 4x100 g a.s./ha in potatoes.

Propamocarb-HCl showed moderate acute toxicity (LD50: >1472 mg a.s./kg bw) and low short-term dietary toxicity (LC50: >4789 mg a.s./kg diet, LDD50: >962 mg a.s./kg bw/d). In a chronic toxicity test, the NOEC was 500 mg a.s./kg diet (NOEL: 33 mg a.s./kg bw/d)

Propamocarb-HCl pass the EU trigger values for acute and long-term exposure (TER_a >42, TER_{lt} 8.3) according to the EU Tier 1 calculations with a application rate of 4x1000 g a.s./ha in potatoes.

3.3.3.3 *Bees*

Fluopicolide showed low oral (LD50: >241 µg a.s./bee) and contact toxicity (LD50: >100 µg a.s./bee).
Propamocarb-HCl showed moderate oral toxicity (LD50: >84 µg a.s./bee) and low contact toxicity (LD50: >100 µg a.s./bee).

Infinito showed low oral (LD50: >204 µg/bee) and contact toxicity (LD50: >143 µg/bee). All hazard quotients for oral and contact exposure are below the trigger of concern (Q_{HO} and Q_{HC} < 50).

3.3.3.4 *Non-target arthropods*

Infinito was tested on parasitoids (*Aphidius rhopalosiphi),* predatory mites (*Typhlodromus pyri)* and leaf dwelling predators (*Crysoperla carnea)* in Tier 1 laboratory acute studies. Effects above the trigger effect level of 30% were seen on both mortality and reproduction at relevant application rates for parasitoids and predatory mites, but not for leaf dwelling predators. LR50 values were 2.48, 3.24 and >6.4 L product/ha, respectively.

Extended laboratory studies with parasitoids (*A. rhopalosiphi),* predatory mites (*T. pyri)* and leaf dwelling predators (*Coccinella septempunctata)* did not show effects above the trigger effect level of 50% at relevant application rates. LR50 values were >8.0, >4.17 and >4.8 L product/ha, respectively). Both the in-field and the off-field HQ values are below the trigger of concern (HQ <2).

3.3.3.5 *Earthworms*

Fluopicolide and the metabolites M-01 and M-03 showed moderate acute toxicity (14d LC50: >500, 750 and >500 mg/kg dws (dry weight soil), respectively). Metabolite M-02 showed low acute toxicity (LC50: >1000 mg/kg dws). In chronic toxicity tests, the NOEC for fluopicolide and M-01 was 62.5 and 250 mg/kg dws, respectively.

Fluopicolide and the metabolites M-01, M-02 and M-03 pass the EU trigger value (≥10) for acute exposure (TER_a >633, 949, >1266 and >633, respectively). Fluopicolide and M-01 pass the EU trigger values for chronic (≥5) exposure (TER_{lt} 79 and 317, respectively).

Propamocarb-HCl showed moderate acute toxicity (14d LC50: >660 mg/kg dws). In a chronic toxicity test the NOEC was 362 mg/kg dws. Propamocarb-HCl pass the EU trigger value for acute (≥10) and chronic (≥5) exposure (TER_a >73, TER_{lt} 40).

Infinito showed moderate acute toxicity (14d LC50: >500 mg product/kg dws). In a chronic toxicity test, the NOEC was ≥30 mg product/kg dws.

3.3.3.6 *Other soil macro-organisms*

Fluopicolide and metabolite M-01 showed low to moderate toxicity to the springtail *Folsomia candida* (28d NOEC: 31.25 and 25.0 mg/kg dws, respectively). Fluopicolide and M-01 pass the EU trigger value for chronic (≥5) exposure (TER_{lt}: 40 and 32, respectively).

3.3.3.7 *Microorganisms*

Separate litter bag studies with relevant concentrations of **fluopicolide** and the metabolite M-01 did not show significant effects on the breakdown of organic matter 1, 3 and 6 months after application.

Fluopicolide and metabolite M-01 showed no effects on the carbon and nitrogen transformation at application rates up to 1.38 and 0.69 kg/ha, respectively (1.84 and 0.92 mg/kg soil).

Propamocarb-HCl showed no effects on the carbon and nitrogen transformation at application rates up to 28.9 kg/ha.

Infinito showed no effects on the carbon and nitrogen transformation at application rates up to 16 L product/ha.

Five different soil fungus strains representative to zygomycetes, oomycetes, deuteromycetes, ascomycetes and basidiomecetes were tested for their sensitivity to **fluopicolide**. Only *Phytophtora nicotianae* (oomycetes) indicated a relative sensitivity to fluopicolide with an EC50 value of 1.2 mg a.s./kg dry soil. This specific sensitivity is expected as *P. nicotianae* is considered as a target organism. As for the aquatic diatoms, this specific sensitivity of oomycetes is explained by the specific mode of action of fluopicolide on zoospores. The other fungus strains were much less sensitive to fluopicolide with EC50 values > 30 mg a.s./kg soil (highest tested concentration). None of the fungus strains revealed to be sensitive to metabolite M-01 with EC50 values >30 mg/kg soil (highest tested concentration).

3.3.3.8 *Terrestrial plants*

Seedling emergence and vegetative vigour studies have been conducted with **Infinito** on 6 species (lettuce, oilseed rape, cucumber, soybean, oats and onion) tested at the maximum application rate of 2.13 L product/ha. The effects were well below the trigger of 50% effect (max 31%). Metabolite M-01 has been tested on seedling emergence to non-target plants. The study showed no effects > 50% on seedling germination and growth at application rates up to 0.0121 mg/kg soil.

3.3.4 EFFECTS ON AQUATIC ORGANISMS

The TER calculations below are based on maximum PEC-values from FOCUS surface water modelling (without extra buffer zones) and the lowest acute (LC50 or EC50) or chronic (NOEC) values for the different organism groups. A tiered approach is applied, where TER based on Step 1 first is calculated. If the TER fails the triggers, Step 2 is calculated and so on. The EU triggers for TER_{acute} (TER_a) and $TER_{long\text{-}term}$ (TER_{lt}) are ≥100 and ≥10, respectively.

3.3.4.1 *Fish*

Fluopicolide showed high acute toxicity (96h LC50: 0.36 mg a.s./L) and moderate chronic toxicity (33d NOEC: 0.155 mg a.s./L). The metabolites M-01, M-02 and M-05 showed low acute toxicity (96h LC50: 240, >102 and >101 mg a.s./L, respectively).

Based on Step 2, TER_a for fluopicolide is calculated to be 35, which fail the EU trigger. Using Step 3 gives a TER_a of 261, which pass the EU trigger. Based on the FOCUS Step 2, TER_{lt} for fluopicolide is 15, which pass the EU trigger. The TER_a for the metabolites M-01 and M-02 also pass the EU trigger (>160 000).

Propamocarb-HCl showed low acute (96h LC50: >92 mg a.s./L) and chronic toxicity (33d NOEC: 6.3 mg a.s./L).

Based on Step 2, TER_a for propamocarb-HCl is >3117, which pass the EU trigger. Using Step 2, TER_{lt} for propamocarb-HCl is 213, which pass the EU trigger.

Infinito was acutely toxic (96h LC50: 6.57 mg/L).

3.3.4.2 *Invertebrates*

Fluopicolide was acutely toxic to *Daphnia magna* (48h EC50: >1.8 mg a.s./L), mysids (96h EC50: 3.2 mg a.s./L) and oysters (96h EC50: 2.6 mg a.s./L), and showed moderate chronic toxicity (21d NOEC: 0.370 mg a.s./L) to *D. magna*. M-01 was acutely toxic to *D. magna* (48h EC50: 180 mg a.s./L).

Based on Step 2, TER_a for fluopicolide is >175, which pass the EU trigger. TER_{lt} for fluopicolide is 35, which pass the EU trigger. TER_a for M-01 is 121 622, which pass the EU trigger.

Propamocarb-HCl showed low acute (48h EC50: >100 mg a.s./L) and chronic toxicity (21d NOEC: 12.3 mg a.s./L) to *D. magna*.

Based on Step 2, TER_a for propamocarb-HCl is >3387, which pass the EU trigger. TER_{lt} for propamocarb-HCl is 271, which pass the EU trigger.

Infinito showed low acute toxicity (48h EC50: >100 mg/L) to *D. magna*.

3.3.4.3 *Sediment dwelling organisms*

Fluopicolide showed low chronic toxicity (28d NOEC: 49 mg a.s./kg) to chironomid larvae in a spiked sediment test.

Based on Step 2, TER_{lt} for fluopicolide is 1470, which pass the EU trigger.

3.3.4.4 *Aquatic plants*

Fluopicolide was acutely toxic to duckweed (7d EC50: >3.2 mg a.s./L). M-01 showed moderate toxicity to duckweed (7d EC50: 80 mg a.s./L).

Based on Step 2, TER_{lt} for fluopicolide is >302, which pass the EU trigger. TER for M-01 is 53 691, which pass the EU trigger.

Propamocarb-HCl showed moderate toxicity to duckweed (7d EC50: >18 mg a.s./L).

Based on Step 2, TER_{lt} for propamocarb-HCl is >397, which pass the EU trigger.

3.3.4.5 *Algae*

Fluopicolide showed extremely high toxicity (72h EbC50: 0.029 mg a.s./L, 72h ErC50: 0.066 mg a.s./L). The metabolites M-01, M-02 and M-05 showed low acute toxicity (72h EC50: >10, >32 and >10 mg a.s./L, respectively).

Based on Step 2, TER for fluopicolide is 2.7, which fail the EU trigger. Using Step 3 gives TER 21, which pass the EU trigger. Using Step 2, TER for the metabolites M-01 and M-03 are >6711 and 74, respectively, which pass the EU trigger.

Propamocarb-HCl is acutely toxic (72h EbC50: >85 mg a.s./L, 72h ErC50: >85 mg a.s./L).

Based on Step 2, TER for propamocarb-HCl is >1874, which pass the EU trigger.

Infinito showed very high toxicity (72h EbC50: 0.40 mg/L, 72h ErC50: 0.63 mg/L).

3.3.4.6 *Microcosm/Mesocosm studies*

No studies submitted.

3.3.5 BIOCONCENTRATION

Log Pow for **fluopicolide** is 2.9. Fluopicolide showed a very rapid absorption in bluegill sunfish (time to 90% steady state was 1.5 days), a bioconcentration factor of 121 and a very rapid depuration halflife (maximum 0.51 days). This indicates a low fish bioaccumulation potential for fluopicolide and also a low potential for secondary poisoning of fish eating birds and wild mammals.

log Pow for **propamocarb-HCl** is -1.3. Bioconcentration factor values for bluegill sunfish were <10, and in channel catfish < 40. In both species, depuration was rapid, e.g. with residues falling below the detection limits after 10 days in bluegill sunfish. Propamocarb-HCl residues in fish are thus not of concern, and no additional residues data are necessary.

3.4 DOSSIER QUALITY AND COMPLETENESS

The dossier is complete and is adequate as a basis for an evaluation of the active substance, metabolites and product.

Draft Assessment Report (DAR), Fluopicolide. *Report and Proposed Decision of the United Kingdom made to the European Commission under Article 8 of Council Directive 91/414/EEC*, November 2005. Chapter B8: Environmental Fate and behaviour and Chapter B9: Ecotoxicology

Draft Assessment Report (DAR), Propamocarb. *Report and Proposed Decision of Ireland made to the European Commission under Article 8 of Council Directive 91/414/EEC*, September 2004. Chapter B8: Environmental Fate and behaviour and Chapter B9: Ecotoxicology

4 Risk characterization

4.1 FATE ASSESSMENT

The Panel on plant protection products of the Norwegian Scientific Committee for Food Safety (VKM) has reviewed the actual documentation and points out the following inherent properties of the product, the active substances and possible metabolites:

4.1.1 Degradation in soil and surface waters

Fluopicolide is relative slowly degraded in soils and from the EFSA document the compound is characterized with a high to very high persistence. Laboratory DT50 values (20 ºC) ranged from 194–411 d while at 10 ºC a DT50 of 667 d was observed. The main metabolite M-01 is also slowly degraded in soils and characterized by EFSA with a very high persistence ($DT_{50\ lab\ 20\ ºC}$ = 557–1831 d). Metabolite M-01 (2,6-Dichlorobenzamide, BAM) is a well-known metabolite also from the active substance dichlobenil. Fluopicolide and the M-01 metabolite also show a high persistence in water and water-sediment systems. VKM supports the view of EFSA and considers both fluopicolide and its main metabolite to be persistent in Norwegian soils and surface waters.

In the submitted field studies, the dissipation behaviour of fluopicolide was found to be bi-phasic, with rapid initial degradation followed by a slower second phase. Estimated DT_{90}–values of 691 to 1184 days far exceeds the duration of the studies

The slow degradation of fluopicolide results in a significant potential for soil accumulation after repeated use. This is to some extent confirmed by calculations with the Finnish PEC calculator, where a plateau concentration was reached at 0.79 mg/kg compared to initial exposure concentration of 0.33 mg/kg. According to EFSA, potential for accumulation of fluopicolide and the metabolite M-01 was confirmed by the PEC soil calculation and plateau concentrations were reached for the parent after 7 years in potatoes and after 9 years in vines and for the metabolite M-01 after 5 years in potatoes and 6 years in vines. VKM concludes that fluopicolide and its main metabolite M-01 may accumulate in Norwegian soils.

4.1.2 MOBILITY IN SOILS

The lysimeter study suggested that there is low potential for fluopicolide and M-02 and M-03 to appear in groundwater. A number of metabolites were detected in concentrations above 0.1 µg/l, but all the metabolites were considered not relevant by EFSA. In the field leaching study metabolite M-01 reached an annual average concentration of 2.9 µg / L in the leachate at 120 cm depth the third year after the product was applied. From the EFSA report modelling with FOCUS PELMO and FOCUS PEARL, fluopicolide and its metabolites M-03, M-01, M-05, M-10, M-11, M-12 and M-13 may exceed the limit of 0.1 µg / L annual average concentration at 1 m depth for at least one of the scenarios simulated, but not for the most relevant scenarios for Norwegian conditions. The metabolite M-01 also exceeded another EU limit of 0.75 µg / L (limit for metabolites of unknown structure (SANCO, 2000)) in a number of scenarios. From ten years of pesticide monitoring Norwegian groundwater wells, during the period from 1995 to 2004 , the metabolite M-01 or 2,6-dichlorobenzamid (BAM) has been reported found in 7 locations and totally 37 times with maximum concentration 1.2µg/L. The groundwater limit on 0.1 µg/L was exceeded 13 times (Haarstad & Ludvigsen, 2007).

From the registration report (E1) half-life for the groundwater simulations are 134 days and 53 days for fluopicolide and M-01 respectively, concluding for most of the simulations no

concern of groundwater contamination. The half-lives are derived and normalized from dissipation studies in field, and in the simulations they use time dependent sorption (aged sorption) which gives much lower values than the values from the laboratory study. From the proposed guidance on how to conduct aged sorption studies, it is recommended not to use column and field studies. Because of the complexity and large uncertainty of these methods, laboratory incubation studies are recommended (Beinum et al. 2010). Especially for highly mobile compounds the guidance recommends not to use field studies.

VKM also recommends that results from laboratory studies are used as input data in fate modelling. VKM concludes that the metabolite M-01 is highly mobile; however fluopicolide shows lower mobility in both studies and modelling.

4.1.3 FATE IN AIR

Fluopicolide has a very low vapour pressure and Henry's Law constant and thus would not be expected to be found in any significant concentration in the air. The theoretical half-life is 2.2 to 3.4 days. However since half-life in the atmosphere is longer than 2 d and fluopicolide is sprayed, formation of aerosols and long range transport trough the atmosphere cannot be complete excluded.

4.2 ENVIRONMENTAL RISK CHARACTERIZATION

The risk characterization of the product's ecotoxicological effects on terrestrial and aquatic organisms made by VKM is based on the summary from the Norwegian Food Safety Authority presented in section 5.3 and exposure-, dose/response assessments and risk scale described in section 5.2.2.

4.2.1 EFFECTS AND RISK TO TERRESTRIAL ORGANISMS

VKM concludes that there is minimal risk for toxic effects of fluopicolide to mammals, birds, bees, earthworms, plants and soil microorganisms with the proposed application regime.

Non-target arthropods

Standard laboratory studies showed effects above the trigger of >30% effect for parasitoids and predatory mites, however extended laboratory studies with parasitoids and predatory mites did not show effects above the trigger effect level of 50 % at relevant application rates. Both the in-field and the off-field HQ values are below the trigger of concern (HQ < 2).

4.2.2 EFFECTS AND RISK TO AQUATIC ORGANISMS

VKM concludes that there is minimal risk for toxic effects of fluopicolide to aquatic organisms with the proposed application regime.

4.2.3 Quality of the submitted documentation

VKM is of the opinion that the submitted documentation is adequate as a basis for an evaluation of the active substance, the metabolites, and for the technical material.

5 Conclusion

The opinion of VKM is that both fluopicolide and its main metabolite M-01 (2,6-dichlorobenzamid (BAM)) are persistent in Norwegian soils and surface waters.

Other conclusions from VKM are as follows:

- Fluopicolide and its main metabolite M-01 may accumulate in Norwegian soils.
- The metabolite M-01 is highly mobile; however fluopicolide shows lower mobility in both studies and modelling.
- There is minimal risk for toxic effects of fluopicolide on terrestrial and aquatic organisms with the proposed application regime.

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