CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance flonicamid[1]

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SUMMARY

Flonicamid is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[3] France received an application from ISK Biosciences for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2004/686/EC[4].

Following the agreement between the EU-Commission and the EFSA for the EFSA to organise a peer review of those new active substances for which the decision on the completeness of the dossier had been published after June 2002, the designated rapporteur Member State France made the report of its initial evaluation of the dossier on flonicamid, hereafter referred to as the draft assessment report (DAR), available on 24 May 2005.

The peer review was initiated on 3 June 2005 by dispatching the DAR (France, 2005) for consultation of the Member States and the applicant. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed on during a written procedure in February – March 2007. Remaining issues as well as further data made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in November 2006, January 2007 and April to May 2009.

A final discussion of the outcome of the consultation of experts took place during a written procedure with Member States (in November 2009) leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide as proposed by the applicant which comprise foliar spraying to control aphids, in the early developmental phase of the population, from early spring till unearly summer, in potatoes, wheat, apples and pears in all EU countries and in peaches in Southern Europe, up to maximum 2-3 treatments per year, at a maximum individual application rate per spray of 70-80 g as/ha with an interval of 21days between applications.

The representative formulated product for the evaluation was 'Teppeki', a water dispersible granule (WG) containing 50% flonicamid.

The technical specification is open waiting for further justification.

Adequate methods are available to monitor all compounds given in the respective residue definitions. Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

1 On request from the European Commission, Question No EFSA-Q-2009-00318, issued on 18 December 2009.
2 Correspondence: praper@efsa.europa.eu
3 OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 20, 22.1.2005, p.19
4 OJ No L 313, 12.10.2004, p. 21
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Flonicamid is rapidly and almost completely absorbed but not extensively metabolised, and excreted mainly via urine. It is harmful after acute oral administration (**Xn R22** "Harmful if swallowed"). After repeated administration, the target organs were the liver, the kidneys and the haematopoietic system. No potential genotoxicity has been shown, and no carcinogenic effect was observed in rats. However in mice, the relevance of lung tumours for humans was not clearly dismissed and the classification has to be discussed by ECHA. No adverse effects on the reproductive parameters were observed in the rat, but indications of foetotoxicity in both rats and rabbits lead to the proposal **Repr.Cat.3 R63?** ("Possible risk of harm to the unborn child":with a question mark). Some metabolites identified in the rat metabolism were tested and considered of lower toxicity than flonicamid. The agreed acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD) are 0.025 mg/kg bw/day, with the use of a safety factor of 100. The dermal absorption values are 7.46% for the concentrate and 13% for the spray dilution. According to the German model, the estimated operator exposure is below the AOEL without the use of personal protective equipment for both applications in field crops and orchards. The worker exposure is 5.7% of the AOEL if standard clothing and gloves are worn. The bystander exposure is < 1% of the AOEL for the use on potatoes and 14% of the AOEL during orchard application.

Metabolism of flonicamid was studied in wheat, potato, peach and additionally on pepper. The metabolism was shown to be comparable in all crops investigated and the residues mainly composed of flonicamid and metabolites TFNG and TFNA, but in significant different ratios depending on the crop. Considering that the additional metabolites TFNA-AM and TFNG-AM are not expected to be present in plants in significant levels, the residue definition for risk assessment was finally limited to the sum of "flonicamid, TFNA, TFNG expressed as flonicamid". Two options were proposed to define the residue for monitoring; as "flonicamid only" or as "sum flonicamid, TFNA; TFNG expressed as flonicamid". The submitted residue trials where samples were analysed for flonicamid, TFNA, TFNG and TFNA-AM, allowed to derive MRLs according the two proposed residue definitions for monitoring, and to derive conversion factor for risk assessment when the residue is defined as the parent compound only.

Metabolism of flonicamid was also studied in livestock. Having regard to the additional excretion study conducted with ^{14}C-TFNA on rat, the experts in the PRAPeR 70 meeting agreed to define the residue for monitoring and risk assessment as "sum flonicamid, TFNA-AM expressed as flonicamid". Based on the feeding studies performed with a mixture 1/1 of flonicamid/TFNG a global MRL of 0.02* mg/kg was proposed for products of animal origin. No rotational crop data were required, the degradation of flonicamid and its metabolites in soil being extremely rapid. The chronic and acute risk assessment performed using the EFSA PRIMO rev.2 model shows consumer exposure below the ADI and ARfD.

In soil under aerobic conditions flonicamid exhibits very low to low persistence rapidly forming the major soil metabolites TFNA, TFNA-OH and TFNG-AM and the minor soil metabolites TFNG and TFNA-AM which also exhibit very low or low persistence. Mineralisation to carbon dioxide accounted for 47-57 % of applied radioactivity (AR) after 30 days (study end). The formation of unextractable residues was also a significant sink accounting for 30-43%AR at study end. Flonicamid and its 5 identified soil metabolites exhibit very high mobility in soil. There was no indication that adsorption of either flonicamid or its 5 identified soil metabolites was pH dependant.

In 2 natural sediment water systems flonicamid dissipated exhibiting moderate persistence in water. In the total system flonicamid also exhibited moderate persistence. In the water phase of 1 system two metabolites were identified TFNA and TFNA-OH as being present at levels that justified their inclusion in the aquatic risk assessment. The terminal metabolite, CO_2, was the most significant degradation product accounting for 16-59 % AR at 136-145 days (study end). Unextracted sediment residues were also a sink for radioactivity representing 38-75 %AR at study end. The necessary surface water and sediment exposure assessments were appropriately carried out using the agreed FOCUS scenarios approach for flonicamid and the five identified metabolites at steps 1 and 2.

The potential for groundwater exposure from the applied for intended uses above the parametric drinking water limit of 0.1µg/L by parent flonicamid and its 5 identified soil metabolites TFNA, TFNA-OH, TFNA-AM, TFNG and TFNG-AM, was concluded to be low, in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios.

The risk to non-target organisms was assessed as low for all groups of non-target organisms. The first-tier HQ values for acute oral and contact exposure of bees were far below the trigger of 50 indicating a low risk. However adverse effects on bees were observed in some of the additionally submitted tunnel tests e.g. altered

feeding behaviour (avoidance) and increased mortality of bees when bees were present during spraying. Therefore the RMS suggested to restrict the use to periods of no flowering for uses in apples/pears and peaches and additional information may be required (bee brood feeding study) if other authorizations e.g. in oilseed-rape are granted at MSs level.

Key words: flonicamid, peer review, risk assessment, pesticide, insecticide

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BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC France received an application from ISK Biosciences for inclusion of the active substance flonicamid in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2004/686/EC.

Following the agreement between the EU-Commission and EFSA for EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the designated rapporteur Member State France submitted the report of its initial evaluation of the dossier on flonicamid, hereafter referred to as the draft assessment report (DAR), to EFSA on 24 May 2005. This DAR (France, 2005) was distributed for consultation to the Member States and the applicant on 3 June 2005.

The comments received on the DAR were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed during a written procedure in February – March 2007 on data requirements to be addressed by the applicant as well as issues for further detailed discussion at expert level.

Taking into account the information received from the applicant addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised in Parma in November 2006, January 2007 and April to May 2009. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States in November 2009 leading to the conclusions as laid down in this report.

During the peer review of the DAR and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR).

Following the agreement between the EU Commission and EFSA regarding the peer review of new active substances, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period. A list of the relevant end points for the active substance as well as the formulation is provided in appendix A.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's DAR:

- the comments received,
- the resulting reporting table (rev. 1-2 of 21 July 2006)

as well as the documents summarising the follow-up of the issues identified as not finalised at the end of the commenting period:

- the reports of the scientific expert consultation,
- the evaluation table (rev. 5.0 of 17 November 2009)

Given the importance of the draft assessment report including its addendum (compiled version of November 2009) containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Flonicamid is the ISO common name for *N*-cyanomethyl-4-(trifluoromethyl)nicotinamide (IUPAC).

Flonicamid belongs to the class of nicotinoid insecticides. Flonicamid exhibits systemic and translaminar activity and inhibits feeding. It is used as a foliar application to control aphids in various agricultural crops.

The representative formulated product for the evaluation was 'Teppeki', a water dispersible granule (WG), containing 50% flonicamid, registered under different trade names in Europe.

The representative uses evaluated comprise foliar spraying to control aphids, in the early developmental phase of the population, in potatoes up to growth stages of BBCH 81-95, in wheat up to growth stages of BBCH 51-85, in apples/pears up to growth stages of BBCH 81-89, in all EU countries, and in peaches up to growth stages of BBCH 81-89 in Southern Europe, up to maximum 2-3 treatments per year, at a maximum individual application rate per spray of 70-80 g as/ha at an interval of 21 days between applications.

CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of flonicamid is 960 g/kg. No FAO specifications is available.

The manufacture of the technical material has been moved from the pilot plant to industrial scale and new five batch data were provided and presented in the Addendum 3 to vol.4 (France, 2009). The technical specification was not changed. The RMS and also the experts of PRAPeR 06 meeting (November 2006) considered that the new data did not support the specification for the impurities and required justification for the limits proposed for the technical specification. The experts of PRAPeR 66 meeting (April 2009) confirmed the data gap as no new specification, or justifications for the proposed limits, were provided. Toluene was considered an impurity of toxicological relevance based on its hazards and the level proposed in the technical specification does not give rise to significant toxicological concern.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of flonicamid or the respective formulation.

The main data regarding the identity of flonicamid and its physical and chemical properties are given in appendix A.

Adequate analytical methods (HPLC-UV) are available for the determination of flonicamid in the technical material and in the representative formulation as well as for the determination of the relevant impurities in the technical material. Sufficient test methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor residues of flonicamid and its metabolites TFNG, TFNA and TFNA-AM in food/feed of plant origin by HPLC-MS/MS with LOQs of 0.01 mg/kg for each compound in wheat grain, tomatoes and apples and with LOQs of 0.02 mg/kg respectively in wheat straw. HPLC-MS/MS method exists also to determine residues of flonicamid and its metabolites TFNG, TFNA and TFNA-AM in peaches and potatoes with LOQs of 0.05 mg/kg for each compound.

Residues of flonicamid and its metabolites TFNA, TFNG, TFNA-AM and OH-TFNA-AM in food of animal origin can be determined by HPLC-MS/MS with LOQs of 0.01 mg/kg for each compound in

bovine, poultry tissues and poultry eggs, LOQs of 0.01 mg/l for milk and LOQs of 0.025 mg/kg for the other ruminant tissues, respectively.

A validated HPLC-MS/MS method is available for the determination of residues of flonicamid and its metabolites TFNG, TFNG-AM, TFNA, TFNA-AM and TFNA-OH in soil with LOQs of 0.005 mg/kg for each compound. Flonicamid, TFNA, TFNG, TFNA-AM, TFNA-OH and TFNG-AM in drinking water and surface water can be determined by HPLC-MS/MS with LOQs of 0.1 µg/L for each compound.

A validated HPLC-UV method is available to determine flonicamid in air with a LOQ of 1.5 µg/m^3.

In conclusion adequate methods are available to monitor all compounds given in the respective residue definitions.

Methods for body fluids and tissues are not required as the active substance is not classified as toxic or very toxic.

2. Mammalian toxicity

Flonicamid was discussed by the experts in mammalian toxicology in the PRAPeR meetings 09 (December 2006), 14 (January 2007) and 69 (May 2009). Several addenda to the section B.6 of Volume 3 were provided during the peer-review: addendum 1 in February 2006, addendum 2 in October 2006, addendum 3 in December 2006, addendum 4 in March 2007, addendum 5 in May 2007 and addendum 6 in September 2007 (France, 2009)

During the expert meetings PRAPeR 09 and 14, the toxicological batches were not confirmed to be representative of the technical material as proposed in the DAR and in the addendum 3 to Vol.4 (France, 2009) with regard to the levels of impurities. Based on the addenda 4, 5 and 6 to Vol.3-B.6 and on the addendum 4 to Volume 4 (France, 2009), the experts agreed during the meeting PRAPeR 69 that the proposed levels of impurities in the technical specification were not of concern from a toxicological point of view (see also section 2.8). However it has to be noted that the final technical specification (large scale production) is not yet agreed (see section 1).

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Flonicamid was rapidly and almost completely absorbed (>80% within 24h) after oral administration. Widely distributed, it did not show accumulation in the carcass. The excretion occurred mainly via urine (70-80% within 24h), but also via faeces (~5%) and bile (~4%). The metabolism was not extensive, flonicamid being the major residue in urine, bile and liver. Among 10 isolated metabolites, the main one was TFNA-AM (~25% in urine).

2.2. Acute toxicity

The acute oral LD_{50} values in the rat were 884 (males) and 1768 (females) mg/kg bw. Accordingly, the classification proposal was **Xn, R22 'Harmful if swallowed'**. There was no toxicity by dermal exposure or by inhalation, no irritating effect to the skin or to the eyes, and no sensitization properties (Magnusson & Kligman test).

2.3. Short term toxicity

The short term effects of flonicamid after oral administration were studied in rats (28 and 90 days), in dogs (28/35 and 90 days, 1 year) and in mice (90 days). Dermal administration was also performed in rats (28 days). The target organs were the liver (rats, mice), the kidney (rats) and the haematopoietic system (anaemia in mice).

In the rat studies, the adverse effects on the kidneys were considered as mediated by the male rat-specific protein, α2µ-globulin, and were not regarded as relevant to humans. Therefore, the short term NOAEL in rats was 60 mg/kg bw/day from the 90-day study. In the dog studies, the relevant NOAEL

was 8 mg/kg bw/day, based on reduced body weight gain, reduced thymus weight in males (90-d), and mild anaemia (1-y). In the mouse study, the NOAEL was 15.3 mg/kg bw/day based on hepatocellular hypertrophy and splenic extramedullary haematopoiesis (related to anaemia).

In a 28-day percutaneous study with rats, the NOAEL was higher than 1000 mg/kg bw/day (highest dose tested).

2.4. Genotoxicity

The genotoxic properties of flonicamid were studied in a battery consisting of three *in vitro* tests (Ames, chromosome aberration and gene mutation) and three *in vivo* tests (micronucleus, UDS and Comet assay). No genotoxic potential has been demonstrated.

2.5. Long term toxicity

Long term studies were performed with rats (one 2-year) and mice (two 18-month).

For the **rat study**, additional details about tumours were been presented in the addendum 3 to B.6 (France, 2009) and discussed by the experts. The lung masses in males at the high dose were described as tumours of various histopathological types and concluded to be not treatment related. The squamous cell carcinomas in the nasal cavity were re-evaluated as occurring in the nasolacrimal duct. They were neither dose-related nor with statistical significance and were observed unilaterally and without preneoplasic lesions. The benign cerebellum granular cell tumours in females at the high dose were considered incidental (probably underreported in the historical control data since they are often only observed microscopically). As a conclusion the experts agreed that flonicamid had no carcinogenic potential in rats, and that the NOAEL for systemic effects was 7.32 mg/kg bw/day.

In the **first mouse study,** adverse effects were observed at the low dose level (29-38 mg/kg bw/day), including non neoplastic effects (in liver, spleen and bone marrow) and neoplastic effects (increased incidences of lung adenoma and carcinoma). In the **second mouse study**, flonicamid induced increased incidences of pulmonary hyperplasia/hypertrophy in the terminal bronchiolar region in both sexes, and an increased incidence of pulmonary adenomas in males at the high dose (30.3 mg/kg bw/day). The NOAEL for lung lesions was 10.0 mg/kg bw/day. Mechanistic studies (see 2.8) and historical data in CD-1 mice indicated that these findings could be species and strain related, and the relevance for humans has been discussed. The experts could not conclude and decided to highlight this issue to ECHA (with regard to classification).

The overall NOAEL for long term toxicity was 7.32 mg/kg bw/day from the 2-year rat study.

2.6. Reproductive toxicity

In the rat multigeneration study, the NOAEL for the reproductive parameters was 109.1 mg/kg bw/day based on the absence of effects on mating, fertility or gestation. Potential anti-oestrogenic effects of flonicamid were discussed by the experts based on additional studies provided in addendum 3 to B.6. The variations observed in some hormone levels in females (reduced 17β-oestradiol, increased LH and FSH) were considered not adverse taking into account the fluctuations of hormone levels in untreated animals at different sampling times and the lack of variations after dietary administration of flonicamid for 28 or 90 days. The parental NOAEL was 18 mg/kg bw/day based on degenerative renal tubular lesions in males, reduced ovary/adrenal weight and renal tubular vacuolation in females. The NOAEL for the offspring was 30 mg/kg bw/day based on delayed vaginal opening and reduced uterus weights in F1 progeny.

In the rat teratology study, the maternal NOAEL was 100 mg/kg bw/day, based on effects observed in the kidneys and liver. The developmental NOAEL was also 100 mg/kg bw/day, related to an increased incidence of skeletal variations, namely extra cervical ribs. Based on a re-evaluation provided in the addendum 3 to B.6 (France, 2009), the experts have discussed the significance of this finding in the

light of the structure (length of the rib). Taking into account the available data from the study, this effect was considered as adverse, even occurring in the presence of slight maternal toxicity.

In the rabbit teratology study, the maternal NOAEL was 7.5 mg/kg bw/day, based on reduced body weight gain. The experts agreed that there were some indications of foetotoxicity at a dose level without maternal toxicity (foetuses with one or more visceral malformations), and the resulting developmental NOAEL was 2.5 mg/kg bw/day.

According to the findings of foetotoxicity observed in both species, the experts agreed that the proposal **Repr. Cat.3, R63? Possible risk of harm to the unborn child** had to be considered by ECHA.

2.7. Neurotoxicity

Flonicamid has no structural relationship to neurotoxicants and therefore, no studies were performed to assess a delayed neurotoxicity.

The compound was assessed for its neurotoxic properties in rats with an acute and a 90-day study.

In both studies, no specific neurotoxic effect was observed in the clinical signs or histopathological findings. The NOAEL for neurotoxicity was 600 mg/kg bw in the acute study, and 625 mg/kg bw/day in the 90-day study.

2.8. Further studies

Mechanistic studies

Five studies based on cell cycle analysis were conducted to investigate the lung tumor induction in the mouse. A dose-related increase was observed in cell proliferation in the epithelial cells of the terminal bronchiolar region of the lung in male and female CD-1 mice. No effect was observed in rats or in other mouse strains. The NOEL for cell proliferation was 12.3 mg/kg bw/day.

This effect was fully reversible within 7 days of the cessation of treatment, and consisted of elongation and hypertrophy/hyperplasia of the Clara cells in the terminal bronchiolar region of the lung but without cytotoxic effect on the activated Clara cells. Thus the pattern of effects suggests a mitogenic effect rather than cytotoxicity.

Metabolites

Some tests were performed with different metabolites of flonicamid:

	Rat oral LD_{50} (mg/kg bw)	Ames test	90-d rat NOAEL (mg/kg bw/d)	Rat metabolite
TFNA	>2000	negative	136	yes
TFNA-AM	>2000	negative	-	yes
TFNG	>2000	negative	135	yes
TFNG-AM	>2000	negative	-	yes
TFNA-OH	>2000	negative	-	not detected

The experts agreed that the reference values set for flonicamid were representing a worst case with regard to these metabolites, which were assumed to be less toxic than the parent compound and not relevant for groundwater.

Impurities

The **impurity 6** has been tested for gene mutations in a bacterial reverse mutation test (see addendum 1 to B.6, France 2009) and did not show any genotoxic properties.

Toluene as an impurity was considered as relevant due to its toxicological properties: it is classified Repr.Cat.3; R63 Possible risk of harm to the unborn child, Xn; R48/20 – 65 Harmful: danger of serious damage to health by prolonged exposure through inhalation. May cause lung damage if swallowed, Xi; R38 Irritating to skin and R67 Vapours may cause drowsiness and dizziness.

Additional results about the **impurity 4** were provided in the addenda 5 and 6 (France, 2009) and discussed by the experts in the meeting PRAPeR 69. This impurity was not acutely toxic in mice after oral administration (oral LD_{50} >3000 mg/kg bw), and was not mutagenic in an *in vitro* gene mutation test (Ames test).

2.9. Medical data

No adverse health effects have been reported in manufacturing plant personnel, and no data on poisoning is available for humans.

2.10. Acceptable daily intake (ADI), Acceptable operator Exposure Level (AOEL) and Acute reference dose (ARfD)

The experts agreed to use the same rabbit developmental study to derive the ADI, the AOEL and the ARfD. The resulting value is 0.025 mg/kg bw/day, with the use of a safety factor of 100.

The experts considered that the margin of safety with regard to the carcinogenic findings in mice was sufficiently high (~1000x).

2.11. Dermal absorption

One *in vitro* study was presented in the DAR. Only the lowest field use dilution (0.4 g flonicamid/L) was tested with human skin samples and gave a dermal absorption value of 7.46%. Results from a new *in vitro* study with the representative formulation were provided in the addendum 2 to B.6 (France, 2009), showing a value of 13% with human skin samples when the highest field use dilution was tested (0.07 g flonicamid/L). Therefore it was agreed to use dermal absorption values of 7.46% for the concentrate and 13% for the dilution.

2.12. Exposure to operators, workers and bystanders

The representative plant protection product Teppeki is a WG (Water dispersible Granules) formulation containing 500 g flonicamid/kg, for use on field crops (cereals, potatoes) and orchards (peach, apple, pear). Revised exposure estimates were provided in the addendum 4 to B.6 (France, 2009).

Operator exposure

According to the intended uses proposed by the applicant, the maximum applied dose is 80 g a.s./ha for field crops and 70 g a.s./ha for orchards, and the minimum volume 200 L. The supported use is of tractor mounted/ trailed boom sprayer (hydraulic nozzles) for field crops or tractor broadcast air assisted sprayers for orchards.

The estimated operator exposure is below the AOEL without personal protective equipment (PPE), according to German model. According to calculations with UK POEM, the operator exposure is below the AOEL when gloves are used during mixing/loading and application for the spray

application to potatoes, but above the AOEL even with the use of gloves for the spraying on orchards. The results are in the following table:

Estimated exposure presented as % of AOEL (0.025 mg/kg bw/day), according to calculations with the German and UK POEM model. The default for body weight of operator is 70 kg in the German model and 60 kg in the UK-POEM model.

	Field crops (potato)		**Orchards (apple/pear)**	
	No PPE:	**PPE**	**No PPE**	**PPE**
German BBA model	39	21	53	46
UK POEM model	324	90	421	283

PPE (personal protective equipment): gloves during mixing/loading and application

EFSA notes that hand-held application in orchards by knapsack sprayers has not been considered as a representative use and may need to be considered at Member State level.

Worker exposure

As a worst case for the re-entry exposure (Krebs et al., 2000), the scenario for orchards was considered with the highest application rate of 80g as/ha (from the use in potatoes, instead of 70 g as/ha for orchards) and a working day of 8h. Using the highest dislodgeable foliar residue found immediately after the third application (France, 2005), and the precautionary default value of 30,000 for the transfer coefficient, the estimated systemic exposure would be 116% of the AOEL if no protective equipment is worn, and 5.7% of the AOEL if workers wear standard clothing and gloves.

Bystander exposure

Assuming that the bystander exposure occurs only by spray drift (values derived from Rautman et al, 2001, as a percentage of the predicted operator exposure within the tractor cab), the exposure estimates are <1% of the AOEL during field application (potatoes), and 14% of the AOEL during orchard application (considering that the bystander is exposed for 6 hours during spraying).

3. Residues

Flonicamid was discussed by the experts in the PRAPeR meetings for residues in Parma in November/December 2006 (PRAPeR 10) and in May 2009 (PRAPeR 70).

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

Metabolism of flonicamid was investigated with ^{14}C ring labelled substance in three crop groups; cereals (wheat), root/tuber crop (potatoes) and fruit crop (peaches), using foliar application at both normal and exaggerated rates when compared to the notified cGAP. The studies were considered to appropriately cover the representative uses in terms of the selected crop groups and the application parameters, even if the PHI in some studies was sometimes longer than recommended in the GAP.

The parent flonicamid was one of the major radioactive residues present in wheat grain, wheat straw, peach fruit and foliage, accounting for 24% to 65% of the TRR. The major detected metabolites were TFNG in wheat grain (39-44% TRR) and TFNA in peach fruit (17-49% TRR). In potato tubers, the parent flonicamid was observed in lower proportions (6-19% TRR) and TFNG and TFNA were found to be the major components of the residues, representing 25% to 39% of the TRR. In addition, conjugates of TFNA were identified in potato tuber and foliage, but for a maximum of 6% TRR. Other minor metabolites, such as TFNG-AM and TFNA-AM, were detected in proportions not exceeding

10% of the TRR. Non-extractable residues did not exceed 20% of the TRR and when a significant portion was not extracted (wheat straw, chaff and grain), further work was done to confirm that the radioactivity was bound in parts to polar sugars and lignin. This metabolite profile was confirmed during the PRAPeR 70 meeting where experts considered an additional metabolism study performed on pepper and presented in the addendum of March 2009 (France, 2009). Parent flonicamid was found to be the main constituent of the residues (47 to 91% TRR), the significant metabolites being TFNG (up to 28% TRR) and to a lower extent, TFNA (4% TRR). The PRAPeR 70 meeting considered the contradictory information provided by one MS, stating that TFNA-AM was the sole compound found in supervised residue trials conducted on pepper and analysed in Hungary. Considering this information was neither confirmed by the new metabolism study on pepper nor by additional residue trials conducted on *Solanaceae* (tomato, pepper) submitted on MS level for national authorisation where only parent was detected in significant levels, it was concluded that flonicamid, metabolites TFNA and TFNG should be considered as the major constituents of the residues in fruit crops. In conclusion, a similar metabolic pathway was observed and all plant group investigated, involving hydrolysis of the –CN and –CONH functional groups and leading to the two major metabolites TFNA and TFNG with some quantitative variations depending on the crops, the major constituent of the residues at the normal dose rate being; flonicamid in cereal straw, peach foliage, pepper fruit and foliage, TFNG in cereal grains and potato tuber and foliage and TFNA in peach fruit.

Based on these studies and considering the conclusion of the PRAPeR 14 meeting on toxicology that the reference values set for flonicamid are also applicable to the flonicamid metabolites, the PRAPeR 70 meeting experts agreed that flonicamid and all metabolites containing the TFNA moiety (TFNA, TFNG, TFNA-AM and TFNG-AM) should be included in the residue definition for risk assessment.

During and after the experts' meeting PRAPeR 70 the RMS expressed some reservation concerning the proposed definition for risk assessment, in particular the inclusion of the metabolites TFNA-AM and TFNG-AM, these two compounds being very minor and their contribution to the overall consumer exposure very poor (France, 2009):

- TFNA-AM accounts for a low percentage of the total radioactivity (0.3 to 6.2% TRR in the normal dose rate studies) and was never found above the LOQ (<0.01 mg/kg) in a total of 64 supervised residue trials performed on the representatives crops (except one positive value on cereal grain). Similar results were obtained on additional crops (citrus, cherries, tomatoes, peas…) where TFNA-AM was never detected or in very few situations at or close to the LOQ (182 negative results out of 187 samples analysed on different commodities).
- TFNG-AM was not analysed in the supervised residue trials (except in some trials on cereal, but with a non-workable LOQ of 0.2 mg/kg), but it was always identified in metabolism studies at similar or lower amounts than TFNA-AM (0.3 to 4.5% TRR). Therefore TFNG-AM is unlikely to be quantified above the LOQ.

Taking into account the argumentation developed by the RMS following the PRAPeR 70 meeting, and considering that TFNG-AM is not expected to be accumulated in plants in significant amounts since it is above all, an intermediate in the metabolic pathway leading to TFNG, EFSA is of the opinion that the final RMS proposal could be accepted and the residue definition for risk assessment limited to "Sum of flonicamid, TFNA and TFNG expressed as flonicamid". This proposal has to be considered provisional since it has not been peer reviewed.

For monitoring, two options were discussed by the PRAPeR 70 of experts:

1 - A majority of experts were of the opinion to limit the residue definition to the parent compound flonicamid only. However this option would make it difficult to derive reliable conversion factors for risk assessment for cereal grains, since parent levels in the residue trials were always/almost below the LOQ. Based on the supervised residue trials and the residue definition for risk assessment limited to the parent +TFNA and TFNG, the RMS derived conversion factors of 2.5, 1.6, 3.0 and 17.5 for apple, peach, potato and wheat grain respectively. These values were proposed after the PRAPeR 70 meeting in the addendum 8 of August 2009 and were not discussed or peer reviewed.

2 - A minority of experts including the RMS, preferred to define the residue for monitoring as "sum of flonicamid, TFNA and TFNG expressed as flonicamid", since a validated analytical method is available to simultaneously analyse all of these compounds. With such a definition, no conversion factors for risk assessment are required. The applicant was however requested to clarify whether TFNA should be considered as a specific flonicamid metabolite or if it could be a common metabolite to other active substances.

A sufficient number of supervised residue field trials were conducted in pome fruit (apple and pear), potato and winter wheat in several Northern and Southern European countries and in Southern Member States on peaches from 1999-2001. Flonicamid was applied in accordance with the critical GAPs. It is noted that potato trials were consistently carried out at a slightly lower application rate than the cGAP (-25%). The residue trials were supported by sufficient storage stability data and reliable analytical methods validated for flonicamid, TFNG, TFNA and TFNA-AM and achieving an LOQ of 0.01 mg/kg for each individual compound. In potato flonicamid and TFNG-AM residues were all below the LOQ and only low residues of TFNG and TFNA (HR 0.03 mg/kg, respectively) were found at the proposed PHI. In wheat grain, residues were mainly composed of TFNG (STMR 0.28 mg/kg) with low amounts of TFNA (STMR 0.03 mg/kg), most of the values for flonicamid and TFNA-AM being below the LOQ. In wheat straw and in peaches only flonicamid and TFNG were significant, while TFNA-AM was always below LOQ, and positive findings of TFNA rarely occurred. In pome fruit however, flonicamid and TFNA were the most abundant residues while TFNG and TFNA-AM residues did not exceed the LOQ. In accordance with the findings of the metabolism studies, the residues levels for the individual analyte vary from crop to crop and were mainly composed of the parent compound, TFNA and TFNG.

Processing studies were provided for wheat and peach. On peaches, the studies were performed with residues below the LOQ in the raw fruits, and then no processing factors were calculated. However, a processing factor of 2.5 was proposed for prune based on an additional study conducted on plum and presented in the addendum 2 of October 2006. On wheat, no concentration of residues was observed and transfer factors for all processed fractions, including whole meal bread, were less than 1. It must be noted that the initial residue levels in grains were however too low to draw any sound conclusion. Having regard to the open point raised in the PRAPeR 10 meeting concerning the analytical methods used in the processing studies, and considering the validation data provided in the addendum 7 of March 2009, the PRAPeR 70 meeting concluded that these analytical methods were fully validated and acceptable for flonicamid, TFNA, TFNG and TFNA-AM.

3.1.2. Succeeding and rotational crops

A study on residues in succeeding crops is not required, since it is not expected that significant residues remain in soil and may be taken up by succeeding crops. The degradation of flonicamid is extremely rapid in soil with a geometric mean DT_{50} of 1 day. Similarly, the degradation of all soil metabolites is very rapid. DT_{50} values ranged between 0.3 and 2.6 days for the metabolites TFNA, TFNA-OH, TFNG, TFNG-AM and TFNA-AM. (Refer to chapter 4.1.2 of this document)

3.2. Nature and magnitude of residues in livestock

The residue trials data indicated that significant residues may occur in crop parts fed to animals. Therefore, livestock studies with ruminants and poultry were required.

In the goat metabolism study, very low total radioactive residue levels were detected in milk and edible tissues following administration of ^{14}C labelled flonicamid over five consecutive days. The test material was rapidly metabolised and excreted. Approximately 49% of the administered dose was excreted via urine and 17-21% via faeces. The residues in milk and in the edible tissues accounted for approximately 1% and 10% of the administered dose, respectively. TFNA-AM was identified as a major metabolite in liver (29% TRR), kidney (31-41% TRR), fat (74% TRR), muscle (42-50% TRR) and milk (97% TRR). TFNA (free acid and an unstable conjugate) was the major metabolite in urine (56-59% TRR) and in faeces (82-88% of TRR). While in urine the unstable conjugate of TFNA was

dominant, it was the free TFNA in faeces. The unchanged parent compound flonicamid was either not detected, or in very low amounts (max 5% TRR). In addition, the metabolite OH-TFNA-AM accounted for approximately 6-7% TRR in liver, kidney and urine and for less than 1.5% TRR in tissue samples, milk and faeces. Flonicamid is rapidly and nearly completely metabolised in goats. Based on these findings, the main metabolic reaction of flonicamid in ruminant is the hydrolysis of the amide function leading to the TFNA-AM metabolite and ring hydroxylation.

In the metabolism study conducted on laying hens, very low total radioactive residues were detected in eggs and edible tissues following administration of ^{14}C labelled flonicamid over five consecutive days. The majority of the administered dose was rapidly excreted; about 67% was recovered in excreta. The residues in eggs and in the edible tissues accounted for approximately 2.4% and 6% of the administered dose, respectively. Upon identification, TFNA-AM was found to be the predominant residue in eggs, liver, muscle, skin and fat (93-97% TRR in all matrices), and also in kidney (76% TRR), while the amounts of flonicamid were negligible in eggs (*ca* 3-4 % TRR) and all edible tissue and organs (<1% of TRR). Also in excreta TFNA-AM residues accounted for the vast majority 77% of TRR. Other metabolites identified in organs and tissues were hydroxy-TFNA-AM and TFNG-AM, but did individually not exceed 3% TRR in any of the samples. Flonicamid is rapidly metabolised and excreted when administered to laying hens. Only a very little amount of the applied dose was recovered in the edible matrices. The main metabolic pathway in laying hens is comparable with that found in lactating goats and involves hydrolysis of -CN and -CONH functional groups of flonicamid. No significant difference in metabolic patterns in the goat as compared to the rat was found and therefore no pig study was required.

The experts of the PRAPeR 10 meeting noted that the metabolism studies in animals have been carried out with flonicamid solely, whereas TFNA and TFNG residues were also found in feed items at significant levels. Since TFNG is an interim-metabolite in the main metabolic pathway to TFNA-AM, the experts agreed that the metabolism study performed with flonicamid is assumed to cover the metabolites formed upon administration of TFNG to livestock. Conve4rsly, however, TFNA being a final metabolite, a possible accumulation in animal tissues may be suspected, since no information was provided on its rate of elimination via TFNA-conjugates. Therefore the experts proposed a data gap for the submission of metabolism studies in goat and hen with TFNA. This point was re-discussed by the PRAPeR 70 meeting, taking into account the new elimination study performed in rat with ^{14}C-TFNA and presented in the addendum 4 of February 2007. After ingestion, TFNA was rapidly and entirely excreted in urine and faeces, confirming that no accumulation is expected in any tissue. This observation is in line with the rat and ruminant metabolism studies performed with the parent flonicamid, where TFNA (free and conjugated) was the predominant compound excreted in urine in faeces (56% to 88% TRR in the goat study). Based on this information, the experts concluded that accumulation of TFNA is not expected in ruminant matrices, and a metabolism study using this metabolite is no longer necessary. For poultry there are still some uncertainties since, in the metabolism study performed with the parent, the vast majority of the residue in the excreta was TFNA-AM (77% TRR), TFNA accounting for 11% TRR only. However, considering the exaggerated dose rate, at which the study was performed (10 mg flonicamid/kg DM) when compared to the estimated residue intake (0.3 mg/kg DM), it was concluded that no further TFNA metabolism study needs to be requested on poultry.

Finally and considering the additional information provided on TFNA, the PRAPeR 70 meeting was of the opinion to defined the residue in products of animal origin for monitoring and risk assessment as “sum of flonicamid and TFNA-AM expressed as flonicamid”.

The dairy cow and poultry feeding studies were performed with a 1/1 mixture of flonicamid/TFNG administered over 28 consecutive days. This composition gave consideration to the residues in cereal straw but does not reflect the composition of residues in potatoes and fruit pomace, where TFNA is a major residue. However since it was concluded that TFNA is rapidly and almost entirely excreted via urine and faeces after ingestion, the feeding studies performed with the mixture of flonicamid/TFNG were considered acceptable to derive MRLs. Milk, eggs and edible tissues were analysed for residue

levels of flonicamid and its metabolites TFNA, TFNA-AM, OH-TFNA-AM and TFNG. Based on these feeding studies and the estimated intakes by animals calculated using the residue levels observed in feed commodities (expressed as sum of flonicamid, TFNA and TFNG) and a default processing factor of 5 for apple pomace, MRLs were proposed at the LOQ (<0.02* mg/kg) for all animal products.

3.3. Consumer risk assessment

A revised consumer risk assessment based on the proposed residue definition for risk assessment including flonicamid+TFNA+TFNG and using the EFSA PRIMo rev.2 model has been submitted in the addendum 8 of August 2009. Different scenarios were envisaged based on the two different residue definitions proposed for monitoring. These evaluations have not been discussed and not been peer reviewed.

- Using the MRL values defined according to the residue definition limited to parent compound only and the conversion factors of 2.5, 1.6, 3.0 and 17.5 proposed for apple, peach, potato and wheat, the maximum calculated TMDI is 63% of the ADI (0.025 mg/kg bw/d) for the WHO cluster B population and an acute exceedence is observed for peach (114% ARfD) and wheat grain (101% ARfD). A refined calculation using the HRs corrected by the appropriate correction factors (0.26 x 1.6 and 0.06 x 17.5 for peach and wheat respectively), gives values for the acute exposure of 99% and 61% of the ARfD.
- The risk assessment performed using the MRLs proposed when the residue for monitoring is defined as "flonicamid+TFNA+TFNG", leads to similar conclusion. The maximum TMDI is 72% of the ADI but an exceedence of the IESTI is observed for peach (119% ARfD) and wheat (116% ARfD). A refined calculation using the HR values for peach and wheat (0.298 and 1.124 mg/kg respectively) shows intakes below the ARfD value (71% and 64% ARfD respectively).

Both scenarios give similar results; TMDI and refined IESI being below the ADI and ARfD values. Chronic and acute intake of residues resulting from the use of flonicamid according to the representative uses is unlikely to present a risk for the consumers.

3.4. Proposed MRLs

The RMS has submitted different MRL proposals in the addendum 8 of August 2009. These proposals were not discussed and not peer reviewed and have to be considered as provisional.

Plant products

Based on the residue trials where samples were analysed for flonicamid, TFNA and TFNG, the RMS calculated two sets of MRLs, depending on the two optional residue definitions for monitoring:

	Residue definition	
	Flonicamid	**Flonicamid+TFNA+TFNG**
- Apple/pear:	0.1	0.2
- Peach:	0.3	0.5
- Potato tuber:	0.01*	0.1
- Wheat grains:	0.1	2.0

Products of animal origin

The estimates of the residue intakes by animals, based on residue levels in feed commodities expressed according to the proposed residue definition for monitoring (flonicamid+TFNA+TFNG-AM), lead to propose a global MRL of 0.02* mg/kg for all animal products.

4. Environmental fate and behaviour

Flonicamid was discussed at the PRAPeR experts' meeting for environmental fate and behaviour (PRAPeR 7) in November 2006 and the PRAPeR evaluation meeting of September 2007.

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

In soil experiments on four different soils with texture varying from sand to loamy sand (pH 6.2-7.2 organic carbon (oc) 0.6-2.7%) carried out under aerobic conditions in the laboratory (20°C, 45% maximum water holding capacity (MWHC)) in the dark, the predominant pathway of flonicamid degradation was microbially intermediated mineralisation (pyridyl ring radiolabel) to carbon dioxide (47-57 % of applied radioactivity (AR) after 30 days, study end). The formation of residues not extracted by acidified water / acetonitrile was also a significant sink for this applied radiolabel (30-43 % AR after 30 days). Three major (>10%AR) metabolites TFNA (formed by hydrolysis of the amide bond), TFNA-OH (hydroxylation of the piridyl ring of TFNA) and TFNG-AM (hydrolysis of the cyanogroup of flonicamid) were measured at maximum levels of 12-36%AR (at 1-3 days); 12-21%AR (at 2-7 days) and 7.8-10.2%AR (at 0.3-2 days) respectively. Two minor (<10%AR) metabolites TFNG (<3.9%AR) and TFNA-AM (7.6%AR) were also identified and their fate and behaviour was investigated further (soil half lives and adsorption determined).

Degradation under anaerobic conditions was not investigated as it is not pertinent to the season of application of the applied for intended uses and this active substance degrades quickly (see section 4.1.2) so would not remain in soil over the autumn / winter period.

In a laboratory soil photolysis study, the rate of degradation on light exposed air dried soil was faster (single first order DT_{50} 22 days under continuous irradiation) than in dark controls (single first order DT_{50} 53 days). Assuming a 12 hour photoperiod the rate of degradation (single first order DT_{50} 45 days) is significantly longer than that measured in the dark higher moisture content aerobic soil incubation experiments where the microbially intermediated hydrolysis reactions would appear to have occurred more readily. No novel metabolites were identified compared to the higher moisture content dark laboratory incubations. The only degradation product identified was TFNG-AM which accounted for 29%AR at study end (15 days).

4.1.2. Persistence of the active substance and their metabolites, degradation or reaction products

The rate of degradation of flonicamid determined in the 4 soils and under the incubation conditions already described at 4.1.1 above gave single first order DT_{50} in the range of 0.7-1.8 days (arithmetic mean 1.1 days, geometric mean 1 day). Flonicamid is considered to exhibit very low to low persistence.

The rate of degradation of the 5 identified flonicamid soil metabolites when applied as test substances on 3 of the 4 soils described at 4.1.1. above (sand to loamy sand pH 5.7-6.9 organic carbon (oc) 0.6-3.2%) under the incubation conditions already described at 4.1.1 above gave low calculated single first order DT_{50} with TFNA and TFNG-AM exhibiting very low persistence ($DT_{50} \leq 1$ day) and TFNA-OH, TFNG and TFNA-AM exhibiting very low to low persistence ($DT_{50} \leq 2.6$ days). (See the table in section 6 below for details of the ranges for each individual compound.) Arithmetic mean values were TFNA 0.4 days, TFNA-0H 1.6 days, TFNG-AM and TFNG 0.5 days and TFNA-AM 1.6 days.

4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

The adsorption / desorption of flonicamid was investigated in four soils. Calculated adsorption $K_d$oc values varied from 2.5 to 8.7 mL/g, indicating that flonicamid exhibits very high mobility in soil (arithmetic mean 5.9mL/g). The adsorption / desorption properties of the 5 identified flonicamid soil

metabolites was studied in 4 soils or 9 soils for TFNA-AM. Adsorption $K_d$oc values were in the range of <3 to 13.2 mL/g indicating that these 5 metabolites exhibit very high mobility in soil. (See the table in section 6 for details of the range of values for each metabolite). Arithmetic mean values were TFNA *ca*. 2mL/g, TFNA-0H *ca*. 3mL/g, TFNG-AM 9.2mL/g, TFNG *ca*. 1.6mL/g and TFNA-AM 6.2mL/g. There was no indication that adsorption of any of these compounds was pH dependant, though this would be very difficult to identify when the measured adsorption was always so minimal.

The meeting of experts discussed if the adsorption study designs were acceptable particularly with respect to the issue of estimating adsorption equilibrium times (that might have been too short) and the use of mercuric chloride to inhibit microbial activity (additional details clarifying the experimental design and deviations from OECD 106 year 2000 guidelines was included in B.8 Addendum 2 of October 2006, that is included in France (2009)). The experts agreed with the assessment of the RMS that as in these cases adsorption is very low, the deviations from the OECD 106 year 2000 study guideline would not be expected to change the Koc values significantly and the expected effect of there being no deviation from this guideline would have been that higher Koc values would be determined. Therefore in the context of this substance and its metabolites it was agreed that these values could be used in the environmental exposure assessments, as the values would be expected to give slightly conservative exposure estimates.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

In laboratory sterile aqueous hydrolysis experiments flonicamid was stable at pH 4, 5 and 7 at environmentally relevant temperatures. At pH 9 flonicamid degraded with a first order DT_{50} estimated at 204 days at 25°C. The major breakdown product formed was TFNG-AM accounting for a maximum of 30.5%AR at study end (120 days). In laboratory sterile aqueous hydrolysis experiments where TFNA was dosed it was stable at pH 4, 5, 7 and 9 even at 50°C. In a laboratory sterile aqueous photolysis experiment at pH 7 flonicamid degradation was minimal over the 15 days of the experiment.

The water-sediment study (2 systems studied at 20°C in the laboratory) demonstrated flonicamid dissipated exhibiting moderate persistence in water (single first order DT_{50} 30-37 days). In the total system flonicamid also exhibited moderate persistence, (single first order DT_{50} were 36-44days). In 1 sediment water system (0.74%oc river system) levels of metabolites remained low (max. 1.5%AR in water and 0.9%AR in sediment). In the second (10.2%oc pond system) TFNA accounted for a maximum of 9.6%AR in water (at 30 days) and 9.2%AR in sediment (at 42 days). TFNA-OH accounted for a maximum of 12.5%AR in water (at 42 days) and 2.2%AR in sediment (after 30 days). Levels of both metabolites declined at subsequent sampling times following these maxima. The terminal metabolite, CO_2, was the most significant degradation product accounting for 16-59% AR at 136-145 days (study end). Residues not extracted from sediment by acidified water / acetonitrile were also a significant sink for radioactivity representing 38-75 %AR at study end.

FOCUS surface water modelling was evaluated up to step 2 (following FOCUS (2001) guidance) in the DAR (France (2005)) for flonicamid and its metabolites TFNA, TFNA-OH, TFNA-AM, TFNG and TFNG-AM and the peer review agreed these PEC for surface water and sediment as appropriate for use in the EU level aquatic risk assessment. (Member States may wish to note that EFSA considers when following agreed EU evaluation procedures, the observed formation amounts for TFNA-AM and TFNG in both soil and sediment water systems are quite a lot lower than would routinely trigger the need for an aquatic exposure assessment.)

4.2.2. Potential for ground water contamination of the active substance their metabolites, degradation or reaction products

Groundwater modelling was available using FOCUS models and scenarios for the applied for intended uses of spring or summer applications to potatoes, wheat, peaches and pome fruit. Simulations were carried out using FOCUSPELMO for flonicamid (see DAR, France (2005) and B.8 Addendum 2 of October 2006, contained in France (2009)) where the flonicamid input values were a first order soil DT_{50} of 1.1 days (arithmetic mean), Koc of 1.6mL/g and 1/n of 0.9 (as a default value). These values are likely to be comparable / more worst case than the values that would be used following FOCUS (2000 and 2006) guidance which would be a geometric mean first order soil DT_{50} of 1.0 day and $K_d$oc of 5.9mL/g. EFSA proposes a 1/n of 1 would have been appropriate for use in simulations (as the use of Kd values, enables it to be justified that a linear isotherm is assumed, such an approach is consistent with the assessments made for other active substances that have been peer reviewed by EFSA). In the simulations the Q10 used was 2.2, the Walker equation coefficient was 0.7. In the available parent flonicamid simulations annual average concentrations in leachate leaving the top 1m soil column were estimated to be <0.001µg/L at all scenarios (significantly less than the parametric drinking water limit of 0.1µg/L). The results of the available modelling were agreed as appropriate for use in the groundwater exposure assessment for parent flonicamid by the peer review.

The peer review had questions over the derivation of the kinetic formation fractions used to calculate PEC groundwater for the five identified soil metabolites TFNA, TFNA-OH, TFNA-AM, TFNG and TFNG-AM. The RMS provided a further assessment of this issue in B.8 Addendum 2 of October 2006 (France 2009). The RMS and experts at the meeting agreed that the available kinetic formation fractions determined by ModelMaker were not reliable enough to be used and therefore the metabolite PEC groundwater presented in the DAR (France (2005))were not reliable. However the experts also agreed with the RMS assessment in B.8 Addendum 2 of October 2006 (France 2009) that because concentrations of the soil metabolites are lower than those of the active substance and that the properties of the metabolites (DT_{50} and Koc) are very similar to those used in the modelling for the active substance ($K_d$oc value used 1.6mL/g), the simulation results for the active substance (annual average concentration in leachate leaving the top 1m soil layer <0.001µg/L) would also be applicable for the metabolites.

The potential for groundwater exposure from the applied for intended uses above the parametric drinking water limit of 0.1µg/L by parent flonicamid and its 5 identified soil metabolites TFNA, TFNA-OH, TFNA-AM, TFNG and TFNG-AM, is therefore concluded to be low, in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios.

4.3. Fate and behaviour in air

The vapour pressure of flonicamid ($9.4x10^{-7}$ Pa at 20°C) means that flonicamid would be classified under the national scheme of The Netherlands as very slightly volatile. The Henry's law constant of $4.2x10^{-8}$ also indicates negligible volatilisation potential from water / soil water. These physico chemical properties indicate volatilisation losses after spraying operations have finished would be expected to be negligible. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half life estimated at 13.7 days. This indicates that any applied flonicamid that did volatilise (for example if aerosols were formed during application), would be expected to be subject to long range atmospheric transport.

5. Ecotoxicology

Flonicamid was discussed at the PRAPeR experts' meeting for ecotoxicology (PRAPeR 08) in November 2006. Flonicamid was again discussed at the PRAPeR experts' meeting for ecotoxicology (PRAPeR 68) based on addendum 2 (France 2009).

5.1. Risk to terrestrial vertebrates

The representative uses of flonicamid are spray applications to control aphids in potatoes, wheat, apples/pears and peaches. The TER calculations for birds resulted in values well above the Annex VI trigger of 10 and 5 for all representative uses indicating a low risk.

The acute TERs for herbivorous and insectivorous mammals were above the trigger for all uses. The long-term TERs were below the trigger of 5 for small herbivorous mammals in apples/pears and peaches. The refined risk assessment presented in the DAR was questioned during the peer-review and a new risk assessment was presented in an addendum. The experts agreed that a NOEL of 25mg/kg bw/d should be used in the long-term risk assessment. Based on the new endpoint the long-term TERs for small herbivorous mammals were above the trigger of 5 without further risk refinement also for the uses in apples/pears and peaches.

The acute risk to birds and mammals from exposure to contaminated drinking water was assessed as low. Long-term TERs based on PECsw values were calculated in the addendum to the DAR. This was not agreed in the expert meeting. However a consensus was reached that the exposure estimate according to the guidance document on birds and mammals leads to an overestimation of the short-term and long-term risk and no agreed approaches are available to refine the risk. Therefore the experts in the meeting agreed that for the timebeing an acute risk assessment is sufficient and that the risk assessment for uptake of contaminated drinking water should be elaborated further when the guidance document is updated.

During the peer-review concerns were raised with regard to potential endocrine disrupting properties of flonicamid. In the expert meeting it was agreed that the long-term endpoints chosen for the risk assessment cover potential endocrine effects and no additional safety factor would be required.

The log Pow of flonicamid is <3 and therefore no risk assessment for secondary poisoning of earthworm- and fish-eating birds and mammals was triggered.

Two major metabolites TFNG and TFNA were found in plants. TFNA was also found in the hen and mammal metabolism studies and hence is covered by the risk assessment for flonicamid. In a hen feeding study flonicamid and TFNA were fed at a ratio of 1:1 up to a concentration of 23 mg/kg feed without causing adverse effects. This concentration exceeds residues in wheat grains by at least a factor of 10. The risk from these plant metabolites is considered to be low.

Overall it is concluded that the risk to birds and mammals is assumed to be low for all representative uses of flonicamid.

5.2. Risk to aquatic organisms

The acute and chronic toxicity of flonicamid and the metabolites TFNA, TFNA-OH, TFNA-AM and TFNG-AM to aquatic organisms is low. The TERs calculated with FOCUstep1 and step2 PECsw were above the Annex VI triggers of 100 and 10 for the use in apples/pears. The highest PECsw values were observed for the use in apples/pears. Therefore the other uses are covered and the risk to aquatic organisms is considered to be low for all representative uses evaluated.

5.3. Risk to bees

The acute oral and contact toxicity to honeybees was low and the HQ values were calculated as <1.6 and <1.5 indicating a low risk to bees. Further studies (tunnel-tests) were submitted. Lethal effects were observed only when bees where present during spraying and mortality was limited to the 1st day after treatment. Some avoidance and modification of foraging behaviour was observed in some studies. Most studies were too short to detect effects on bee-brood. In one study egg-laying of the queen was stopped but recovery occurred later. Overall it is concluded that the risk to honeybees is low for the uses in potatoes and wheat. However the RMS suggested to restrict the use to periods of no

flowering for uses in apples/pears and peaches and additional information may be required (bee brood feeding study) if other authorizations e.g. in oilseed-rape are granted at MSs level.

5.4. Risk to other arthropod species

Standard laboratory tests on glass plates were conducted with *Aphidius rhopalosiphi*, *Typhlodromus pyri* and *Coccinella septempunctata*. An in-field risk to non-target arthropods was detected in a first tier risk assessment from the representative uses. Higher tier tests (extended laboratory tests) were conducted with the aforementioned species and with *Chrysoperla carnea*, *Episyrphus balteatus*, and *Poecilus cupreus*. No effects of≥ 50% were observed when the arthropods were exposed to fresh residues of an application rate equivalent to 85 g a.s./ha. The application rate of 85 g a.s./ha is about 10-times the rate calculated for the off-field area indicating a low risk to non-target arthropods in the off-field area. However the applied rate was too low to cover the in-field risk to non-target arthropods from the intended uses.

The in-field risk to non-target arthropods was re-assessed in addendum 2 (February 2009). It was evident from residue studies that flonicamid declined very fast from cucumber and potato leaves (DT50 < 1 day). Based on the short dissipation rate and an intended spraying interval of 21 days it was considered that no accumulation of residues on foliage was to be expected (i.e. multi application factor = 1) and the exposure in the existing extended laboratory studies was sufficient to address the in-field risk for the intended uses. In addition the applicant submitted an laboratory study with *Orius laevigatus* exposed to 161 g a.s./ha (dry residues). Effects on *O. laevigatus* were below the Annex VI trigger with two times the expected in-field exposure, adding further certainty to the conclusion of low risk to non-target arthropods from the intended uses.

5.5. Risk to earthwoms

No statistically significant effects were detected in an acute test with flonicamid (technical) and earthworms (*Eisenia foetida*) up to the highest tested concentration of 1000 mg a.s./kg soil. The TER calculation was based on a LC_{50} value of > 1000 mg a.s./kg soil and a maximum PEC soil of 0.0533 mg a.s./kg soil. The corresponding TER value of > 1876 is far above the Annex VI trigger value, indicating a low risk to earthworms from the representative uses. A limit test was conducted with the soil metabolites TFNA, TFNA-OH, TFNG-AM, TFNA-AM at a concentration of 100 mg/kg soil. No statistically significant effects were observed except for TFNG-AM. However, the observed effect (reduction in the mean body weight) was relatively low (12% at a dose of 100 mg TFNG-AM) and the DT_{90} of the metabolite in soil is short (mean DT_{90} of 4 soils = 1.6 d, longest DT_{90} 3.3 days). Since the maximum PECsoil for TFNG-AM was about 5 orders of magnitude less than the tested concentration the margin of safety is considered to be sufficient to conclude that the risk to earthworms is low.

5.6. Risk to other soil non-target organisms

The DT_{90} values (n = 4 soils) determined in laboratory studies for flonicamid, TFNA, TFNA-OH, TFNG-AM, TFNA-AM, and TFNG were in the range of 0.4 to 9 days. Therefore no further testing with other soil non-target organisms is required.

5.7. Risk to soil non-target micro-organisms

The effects on soil respiration and nitrification was tested with the formulation IKI-220 50% WG at dose rates of 0.104 and 0.274 mg product/kg soil (equivalent to 0.053 and 0.14 mg a.s./kg soil). The lower dose rate corresponds to a single application of 80 g a.s./ha and the second to 3 applications of 70 g a.s./ha assuming 50 % foliage interception. No statistically significant effects of > 25 % were observed at either dose rate. Therefore the risk posed to soil non-target micro-organisms is considered to be low from the representative uses.

5.8. Risk to other non-target organisms (flora and fauna)

The effects of the formulation IKI-220 50WG on non-target plants was tested with eleven plant species (beet, lettuce, maize, melon, oat, oilseed rape, pea, soybean, eggplant, pepper and wheat) at a

dose rate of 100 or 200 g. a.s./ha. The effects on succeeding crops was tested with 17 plant species on soil treated with IKI-220 50WG at 100 and 300 g a.s./ha. The seeds of beet, cucumber, eggplant, lettuce, maize, melon, oat, oilseed rape, pea, pepper, soybean, wheat, turnip kidney bean, flax, onion and barley were sown in treated soil. No phytotoxicity was observed in either test indicating a low risk to non-target plants from the representative uses.

5.9. Risk to biological methods of sewage treatment

The toxicity of the formulation IKI-220 50% WG was tested with activated sewage sludge at concentrations ranging from 12 to 1000 mg/L. No significant inhibitory effects on the respiration rate were observed up to the highest tested concentration of 1000 mg/L. Therefore the risk to sewage treatment plants from the representative uses is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: flonicamid, TFNA, TFNA-OH, TFNG-AM, TFNG,TFNA-AM

Definitions for monitoring: flonicamid

Water

Ground water

Definitions for exposure assessment: flonicamid, TFNA, TFNA-OH, TFNG-AM, TFNG, TFNA-AM

Definitions for monitoring: flonicamid

Surface water

Definitions for risk assessment: water: flonicamid, TFNA and TFNA-OH. Potentially originating from soil by runoff or drainage TFNG-AM
sediment: flonicamid

Definitions for monitoring: flonicamid

Air

Definitions for risk assessment: flonicamid

Definitions for monitoring: flonicamid

Food of plant origin

Definitions for risk assessment: sum flonicamid, TFNG, TFNA expressed as flonicamid

Definitions for monitoring: Option 1: flonicamid
Option 2: sum flonicamid, TFNG, TFNA expressed as flonicamid

Food of animal origin

Definitions for risk assessment: sum flonicamid, TFNA-AM expressed as flonicamid

Definitions for monitoring: sum flonicamid, TFNA-AM expressed as flonicamid

7. Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

7.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Compound (name and/or code)	Persistence	Ecotoxicology
flonicamid	Very low to low persistence ($DT_{50\ lab}$ = 0.7-1.8 d, 20°C, 45% MWHC)	LC50 > 1000 mg per kg, low risk to earthworms and soil micro-organisms
TFNA	Very low persistence ($DT_{50\ lab}$ = 0.3-0.5 d, 20°C, 45% MWHC)	LC50 > 100 mg per kg, low risk to earthworms
TFNA-OH	Low persistence ($DT_{50\ lab}$ = 1-2.6 d, 20°C, 45% MWHC)	LC50 > 100 mg per kg, low risk to earthworms
TFNG-AM	Very low persistence ($DT_{50\ lab}$ = 0.2-1 d, 20°C, 45% MWHC)	LC50 > 100 mg per kg, low risk to earthworms
TFNG	Very low to low persistence ($DT_{50\ lab}$ = 0.1-1.1 d, 20°C, 45% MWHC)	Low risk to earthworms
TFNA-AM	Low persistence ($DT_{50\ lab}$ = 1-2.6 d, 20°C, 45% MWHC)	LC50 > 100 mg per kg, low risk to earthworms

7.2. Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
flonicamid	Very high mobility (K_doc =	No	Yes	Yes	Low toxicity and low risk

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
	2.5-8.7 mL/g)				to aquatic organisms
TFNA	Very high mobility ($K_d$oc = <3 mL/g)	No	No information submitted, no data required	No	Low toxicity and low risk to aquatic organisms
TFNA-OH	Very high mobility ($K_d$oc = <4.4 mL/g)	No	No information submitted, no data required	No	Low toxicity and low risk to aquatic organisms
TFNG-AM	Very high mobility ($K_d$oc = 5.5-13.2 mL/g)	No	No information submitted, no data required	No	Low toxicity and low risk to aquatic organisms
TFNG	Very high mobility ($K_d$oc = <4 mL/g)	No	No information submitted, no data required	No	Low toxicity and low risk to aquatic organisms
TFNA-AM	Very high mobility ($K_d$oc = 2.8-12.1 mL/g)	No	No information submitted, no data required	No	Low toxicity and low risk to aquatic organisms

7.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
flonicamid	Low toxicity and low risk to aquatic organisms
TFNA (water only)	Low toxicity and low risk to aquatic organisms

TFNA-OH (water only)	Low toxicity and low risk to aquatic organisms
TFNG-AM (water only originating from soil)	Low toxicity and low risk to aquatic organisms

7.4. Air

Compound (name and/or code)	Toxicology
flonicamid	low acute toxicity by inhalation (rat LC_{50} >4.9 mg/L)

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- New technical material specification or a justification and quality data support the available technical specification (relevant for all representative uses evaluated; identified by RMS, confirmed by PRAPeR expert meetings 6 (September 2006) and 66 (April 2009); submission date unknown, refer to chapter 1)

- Applicant to clarify if the TFNA is a specific flonicamid metabolite or if it could be a common metabolite to other active substances (relevant for all the representative uses, data gap identified in the meeting of experts PRAPeR 70, Information already submitted but not evaluated, refer to point 3.1)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as proposed by the applicant which comprises foliar spraying to control aphids, in the early developmental phase of the population, in potatoes up to growth stages of BBCH 81-95, in wheat up to growth stages of BBCH 51-85, in apples/pears up to growth stages of BBCH 81-89, in all EU countries, and in peaches up to growth stages of BBCH 81-89 in Southern Europe, up to maximum 2-3 treatments per year, at a maximum individual application rate per spray of 70-80 g as/ha at a 21-day interval.

The representative formulated product for the evaluation was 'Teppeki', a water dispersible granule (WG), registered under different trade names in Europe.

Adequate methods are available to monitor all compounds given in the respective residue definitions.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible.

During the expert meetings PRAPeR 09 and 14, the toxicological batches were not confirmed to be representative of the technical material as proposed in the DAR and in the addendum 3 to Vol.4 (France, 2009) with regard to the levels of impurities. Based on the addenda 4, 5 and 6 to Vol.3-B.6 and on the addendum 4 to Volume 4 (France, 2009), the experts agreed during the meeting PRAPeR 69 that the proposed levels of impurities in the technical specification were not of concern from a toxicological point of view (see also section 2.8). However it has to be noted that the final technical specification (large scale production) is not yet agreed (see section 1).

Flonicamid is rapidly and almost completely absorbed but not extensively metabolised, being excreted mainly via urine. It is harmful after acute oral administration (**Xn R22** Harmful if swallowed). After repeated administration, the target organs were the liver, the kidneys and the haematopoietic system. No potential genotoxicity has been shown, and no carcinogenic effect was observed in rats. However in mice, the relevance of lung tumours for humans was not clearly dismissed and the proposal for classification has to be discussed by ECHA. No adverse effects on the reproductive parameters were observed in the rat, but indications of foetotoxicity in both rats and rabbits lead to the proposal **Repr.Cat.3 R63?** Possible risk of harm to the unborn child (with a question mark). Some metabolites identified in the rat metabolism were tested and considered of lower toxicity than flonicamid. The agreed acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD) are 0.025 mg/kg bw/day, with the use of a safety factor of 100. The dermal absorption values are 7.46% for the concentrate and 13% for the spray dilution. According to the German model,

the estimated operator exposure is below the AOEL without the use of personal protective equipment for both applications in field crops and orchards. The worker exposure is 5.7% of the AOEL if standard clothing and gloves are worn. The bystander exposure is < 1% of the AOEL for the use on potatoes and 14% of the AOEL during orchard application.

Metabolism of flonicamid was studied in wheat, potato, peach and additionally on pepper. The metabolism was shown to be comparable in all crops investigated and the residues mainly composed of flonicamid and metabolites TFNG and TFNA, but in significant different ratios depending on the crop. Considering that the additional metabolites TFNA-AM and TFNG-AM are not expected to be present in plants in significant levels, the residue definition for risk assessment was finally limited to the sum of "flonicamid, TFNA, TFNG expressed as flonicamid". Two options were proposed to define the residue for monitoring; as "flonicamid only" or as "sum flonicamid, TFNA; TFNG expressed as flonicamid". The submitted residue trials where samples were analysed for flonicamid, TFNA, TFNG and TFNA-AM, allowed to derive MRLs according the two proposed residue definitions for monitoring, and to derive conversion factor for risk assessment when the residue is defined as the parent compound only. Metabolism of flonicamid was also studied in livestock. Having regard to the additional excretion study conducted with ^{14}C-TFNA on rat, the PRAPeR 70 experts agreed to define the residue for monitoring and risk assessment as "sum flonicamid, TFNA-AM expressed as flonicamid". Based on the feeding studies performed with a mixture 1/1 of flonicamid/TFNG a global MRL of 0.02* mg/kg was proposed for products of animal origin. No rotational crop data were required, the degradation of flonicamid and its metabolites in soil being extremely rapid. The chronic and acute risk assessment performed using the EFSA PRIMO rev.2 model shows consumer exposure below the ADI and ARfD.

The information available on the fate and behaviour in the environment is sufficient to carry out an appropriate environmental exposure assessment at the EU level. For the applied for intended uses, the potential for groundwater exposure by flonicamid or its 5 identified soil metabolites TFNA, TFNA-OH, TFNA-AM, TFNG and TFNG-AM above the parametric drinking water limit of 0.1µg/L, is low.

The risk to non-target organisms was assessed as low for all groups of non-target organisms. The first-tier HQ values for acute oral and contact exposure of bees were far below the trigger of 50 indicating a low risk. However adverse effects on bees were observed in some of the additionally submitted tunnel tests e.g. altered feeding behaviour (avoidance) and increased mortality of bees when bees were present during spraying. Therefore the RMS suggested to restrict the use to periods of no flowering for uses in apples/pears and peaches and additional information may be required (bee brood feeding study) if other authorizations e.g. in oilseed-rape are granted at MSs level.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

- Use of personal protective equipment is needed for re-entry workers in order to have a predicted worst-case exposure level below the AOEL (refer to point 2.12).
- In order to mitigate the risk to bees it is suggested to restrict the use to periods of no flowering for uses in apples/pears and peaches (refer to point 5.3)

ISSUES THAT COULD NOT BE FINALIZED

- No operator exposure estimates were provided for hand-held application in orchards by knapsack sprayers; this may need to be considered at Member State level for the national authorization.
- The technical material specification is not finalized.

CRITICAL AREAS OF CONCERN

None proposed

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APPENDICES

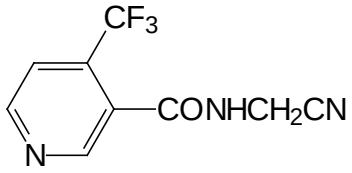
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Flonicamid
Function (e.g. fungicide)	Insecticide / aphicide

Rapporteur Member State	France
Co-rapporteur Member State	UK

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	*N*-cyanomethyl-4-(trifluoromethyl)nicotinamide
Chemical name (CA) ‡	*N*-(cyanomethyl)-4-(trifluoromethyl)-3-pyridincarboxamide
CIPAC No ‡	763
CAS No ‡	158062-67-0
EC No (EINECS or ELINCS) ‡	not allocated
FAO Specification (including year of publication) ‡	No FAO specification is available
Minimum purity of the active substance as manufactured ‡	minimum 960 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Toluene max 3 g/kg
Molecular formula ‡	$C_9H_6F_3N_3O$
Molecular mass ‡	229.16 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	157.5°C (99.7%)
Boiling point (state purity) ‡	No boiling point observed (99.7%)
Temperature of decomposition (state purity)	306-320°C (99.7%)
Appearance (state purity) ‡	PAI : off white: Solid powder, odourless TGAI : Light beige (21°C), solid powder (24.9°C)
Vapour pressure (state temperature, state purity) ‡	2.55×10^{-6} Pa at 25°C 9.43×10^{-7} Pa at 20°C (99.7%)
Henry's law constant ‡	4.2 ×10-8 (20°C) (99.7%) calculation based
Solubility in water (state temperature, state purity and pH) ‡	5.2 g/L at 20°C (99.7%)

Solubility in organic solvents ‡ (state temperature, state purity)

	PAI (99.7%) g/L at 20°C	TGAI (98.7%) g/L at 20°C
Acetone	163.5	157.1
Ethyl acetate	34.2	34.9
Methanol	104.3	89.0
Dichloromethane	4.5	4.0
Toluene	0.55	0.30
Hexane	0.0002	0.0003
n-Octanol	3.0	2.6
Acetonitrile	132.8	111.4
Isopropyl alcohol	18.7	14.7

Surface tension ‡ (state concentration and temperature, state purity)	47.3 mN/m at 25±1°C 47.0 mN/m at 40±1°C Concentration tested 90 % of water solubility. Although the concentration tested is not correct as it is greater than 1 g/L it is clear that the material is surface active. Surface active (98.7%)
Partition co-efficient ‡ (state temperature, pH and purity)	Log P_{ow} = -0.24 at 20°C (pH not measured) (calculated value)
Dissociation constant (state purity) ‡	pKa = 11.6 at 20 ±1°C (99.7%)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	λmax — ε (L/(cm x mol)) 265 nm in neutral solution (99.7%) — 3870 266 nm in acidic solution — 3890 204 and 270 nm in basic solution — 13200 and 4190 No significant absorption above 290 nm
Flammability ‡ (state purity)	Not highly flammable (98.7%)
Explosive properties ‡ (state purity)	Not explosive (expert statement)
Oxidising properties ‡ (state purity)	Not oxidizing (expert statement)

Summary of representative uses evaluated (name of active substance or the respective variant)*

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage&season (j)	number min/max (k)	interval between application s (min)	g as/hL min–max (l)	water L/ha min–max	g as/ha min–max (l)		
Potatoes	all EU countries	Teppeki	F	Aphids	50 WG	500 g/kg	foliar application	maturation of tubers (j). Late spring till early summer. BBCH 81-95	2	21 days	16 - 40	200 - 500	80	14	-
Wheat	all EU countries	Teppeki	F	Aphids	50 WG	500 g/kg	foliar application	ears stage (j) late spring till early summer. BBCH 51-85	2	21 days	14 - 35	200 - 500	70	28	-
Apples/ pears	all EU countries	Teppeki	F	Aphids	50 WG	500 g/kg	foliar application	maturation of fruits (j) early spring till early summer. BBCH 81-89	3	21 days	7 (4.7) – 35	200 - 1000 (1500 excep.)	70	21	-
Peaches	Southern countries	Teppeki	F	Aphids	50 WG	500 g/kg	foliar application	maturation of fruits (j) very early spring till early summer. BBCH 81-89	2	21 days	7 (4.7) – 35	200 - 1000 (1500 excep.)	70	14	-

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).
(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
(c) e.g. biting and suckling insects, soil born insects, foliar fungi, weeds
(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated
(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(m) PHI - minimum pre-harvest interval

Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	HPLC/UV
Impurities in technical as (analytical technique)	HPLC/UV, GC/FID and Karl Fisher titration
Plant protection product (analytical technique)	HPLC/UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Option 1: flonicamid Option 2: flonicamid, TFNA and TFNG expressed as flonicamid
Food of animal origin		flonicamid and TFNA-AM expressed as flonicamid
Soil		flonicamid
Water	surface	flonicamid
	drinking/ground	flonicamid
Air		flonicamid

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC-MS/MS LOQ : 0.01 mg/kg (wheat grain, tomatoes and apples) and 0.02 mg/kg in wheat straw for each compound (flonicamid and its metabolites TFNG, TFNA and TFNA-AM) And HPLC-MS/MS LOQ : 0.05 mg/kg (peach and potatoes) and 0.10 mg/kg (wheat straw) for each compound (flonicamid and its metabolites TFNG, TFNA and TFNA-AM)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC-MS/MS (an enforcement method is not required due to the fact that no MRLs are proposed) LOQ: 0.01 mg/L for milk LOQ: 0.01 mg/kg for bovine, poultry tissues and poultry eggs LOQ: 0.025 mg/kg for the other ruminant tissues for each compound (flonicamid and its metabolites OH-TFNA-AM, TFNA AND TFNA-AM)
Soil (analytical technique and LOQ)	HPLC-MS/MS LOQ: 0.005 mg/kg (flonicamid, TFNG, TFNG-AM, TFNA, TFNA-AM and TFNA-OH)

Water (analytical technique and LOQ)	HPLC-MS/MS LOQ: 0.1 µg/L (flonicamid, TFNA, TFNG, TFNA-AM, TFNA-OH and TFNG-AM in drinking water and surface water)
Air (analytical technique and LOQ)	HPLC-UV LOQ: 1.5 µg/m^3 (flonicamid)
Body fluids and tissues (analytical technique and LOQ)	Not required; the active substance is not classified as toxic or very toxic.

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	none

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	Rapid and extensive > 80% within 24 h Tmax = 0.4 h at low dose (2 mg/kg)
Distribution ‡	Extensive with peak tissue concentrations ≤ peak blood concentrations except in liver, kidney, adrenals, thyroid and GI tract.
Potential for accumulation ‡	None
Rate and extent of excretion ‡	Rapid mostly via urine 70 – 80% within 24 h; low biliary excretion (~ 5% AD).
Metabolism in animals ‡	Proceeds in the rat by nitrile & amide hydrolysis, N-oxidation, hydroxylation of pyridine ring Main component in urine, faeces and bile: IKI-220 (up to 70% AD); main metabolite in urine and bile: TFNA-AM (up to 27% AD); minor metabolites: TFNA and conjugates, TFNG-AM, TFNA-AM N oxide conjugate, OH-TFNA-AM, TFNG
Toxicologically relevant compounds ‡ (animals and plants)	Parent substance
Toxicologically relevant compounds ‡ (environment)	Parent substance, impurity toluene

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	884 – 1768 mg/kg bw (m – f)	**R22**
Rat LD_{50} dermal ‡	> 5000 mg/kg bw	-
Rat LC_{50} inhalation ‡	> 4.9 mg/L (4 h, nose-only aerosol) (MMAD 4.8 µm)	-
Skin irritation ‡	non irritant	-
Eye irritation ‡	non irritant	-
Skin sensitisation ‡	not sensitising (M & K test)	-

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	kidney (rat, dog), liver (mouse, rat), haematopoietic system (mouse, dog)	
Relevant oral NOAEL ‡	8 mg/kg bw/d (dog 90-d and 52 w) 60 mg/kg bw/d (rat, 90-d) 15.3 mg/kg bw/d (mouse, 90-d)	-
Relevant dermal NOAEL ‡	1000 mg/kg bw/d (rat, 28-day study)	-
Relevant inhalation NOAEL ‡	no study – not required	-

Genotoxicity ‡ (Annex IIA, point 5.4)

No genotoxic potential	

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Rat: kidneys, liver, anaemia Mouse: lungs, liver, haematopoietic system	
Relevant NOAEL ‡	7.32 mg/kg bw/d (rat, 2-y) 10 mg/kg bw/d (mouse, 18-month)	
Carcinogenicity ‡	Rat: nasal tumours not considered relevant for humans. Mouse: strain- and species-specific lung tumours of unknown relevance to humans	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Reproduction: no adverse effect on reproductive parameters Parents: kidneys lesions, reduced ovary/adrenal weights Offspring: delayed vaginal opening and reduced uterus weight in F1 weanlings	-
Relevant parental NOAEL ‡	18 mg/kg bw/d	
Relevant reproductive NOAEL ‡	109 mg/kg bw/d (highest dose tested)	
Relevant offspring NOAEL ‡	30 mg/kg bw/d	

Developmental toxicity

Developmental target / critical effect ‡	Development (rat): increased placental weight, increased skeletal variations (cervical ribs) Development (rabbit): increased visceral anomalies without maternal toxicity Parental : liver and kidney (rat), reduced weight gain and food consumption (rabbit)	
Relevant maternal NOAEL ‡	Rat: 100 mg/kg bw/d Rabbit: 7.5 mg/kg bw/d	
Relevant developmental NOAEL ‡	Rat: 100 mg/kg bw/d Rabbit: 2.5 mg/kg bw/d	**Repr .Cat. 3** **R63 ?**

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	NOAEL 600 mg/kg bw (rat)	
Repeated neurotoxicity ‡	NOAEL > 625 mg/kg bw/d (rat, 90-day)	
Delayed neurotoxicity ‡	No study – Not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Lung cell cycle analysis (BrdU index): dose response relationship in the mouse (NOEL 12.3 mg/kg bw/d); reversibility study; comparative study in the rat and the mouse Lung cell cycle analysis (BrdU index) with TFNG, TFNA, TFNA-AM: no effect on BrdU index after a 3 or 7-d treatment at 318-402 mg/kg bw/d Comparison of lung cell cycle analysis after flonicamid or isoniazid dietary exposure in 3 mouse strains: BrdU index increased in CD-1 mouse strain only after flonicamid and no strain specificity after isoniazid.
Studies performed on metabolites or impurities ‡	Acute oral toxicity of metabolites TFNA oral LD_{50}: >2000 mg/kg. No clinical signs TFNA-AM oral LD_{50}: >2000 mg/kg. No clinical signs TFNA-OH oral LD_{50}: >2000 mg/kg. No clinical signs TFNG oral LD_{50}: >2000 mg/kg. No clinical signs TFNG-AM oral LD_{50}:>2000 mg/kg. No clinical signs Genotoxicity testing of metabolites Bacterial reverse mutation assays: negative for TFNA; TFNA-AM; TFNA-OH; TFNG and TFNG-AM. 90-day toxicity studies on metabolites TFNA: NOAEL 136 mg/kg bw/d TFNG: NOAEL 135 mg/kg bw/d

Medical data ‡ (Annex IIA, point 5.9)

Not applicable. Flonicamid has not been marketed. No adverse health effects have been reported in manufacturing plant personnel

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.025mg/kg/d	Rabbit developmental	100
AOEL ‡	0.025mg/kg/d	Rabbit developmental	100
ARfD ‡	0.025mg/kg	Rabbit developmental	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

TEPPEKI® 50% WG	concentrate: 7.46 %; spray dilution: 13 %

Exposure scenarios (Annex IIIA, point 7.2)

		Potato		Orchard	
Operator		no PPE	PPE	no PPE	PPE
	UK POEM	324	90	421	283
	German	39	21	53	46
	PPE: gloves during mixing/loading and application				
Workers	Worst case exposure without PPE: 116% of AOEL; with PPE: 5.7% of AOEL				
Bystanders	Potato scenario: exposure <1% of AOEL Orchard scenario: exposure is 14% of AOEL				

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Flonicamid	Xn R22, Repr.Cat.3 R63

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plants groups covered	Cereals (wheat), Root vegetable (potato) and Fruit crop (peach, pepper)
Rotational crops	none
Plant residue definition for monitoring	Option 1: Flonicamid Option 2: Flonicamid+TFNG+TFNA expressed as flonicamid
Plant residue definition for risk assessment	Flonicamid+TFNG+TFNA expressed as flonicamid
Conversion factor (monitoring to risk assessment)	Option 1: Yes, 2.5 apple/pear, 1.6 peach, 3.0 potato and 17.5 wheat grain Option 2: None

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Goat and hen
Animal residue definition for monitoring	Flonicamid+TFNA-AM expressed as Flonicamid
Animal residue definition for risk assessment	Flonicamid+TFNA-AM expressed as Flonicamid
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue (yes/no)	No

Residue in succeeding crops

Study not required

Stability of residues

Stable for at least a period of 18 months on crops (apple, potato, wheat) and for at least 15 months on cereal products (bread) Stable for a period of at least 8 month in poultry matrices (meat, eggs, fat) and at least 9 month in goat matrices (meat, milk, fat)

Residues from livestock feeding studies

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

	Ruminant:	**Poultry:**	**Pig:**
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes 0.46 and 0.64 mg/kg DM (dairy&beef	Yes 0.33 mg/kg DM Poultry	Yes 0.37mg/kg DM Pig

	cattle)		
Potential for accumulation (yes/no):	No	No	Not applicable
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	Not applicable
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices (flonicamid + TFNA-AM): Max. mg/kg		
Muscle	<0.025 (4 N)	0.050	Not required
Liver	<0.025 (4 N)	0.058 (8 N)	Not required
Kidney	<0.025 (4 N)	-	Not required
Fat	<0.005 (6 N)	0.0226 (8 N)	Not required
Milk	<0.01* (5 N)	-	
Eggs	-	0.0735 (8 N)	

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern/Southern Region	Trials results relevant to the representative uses	Recommendation/ comments	**MRL** estimated from trials according to the representative use	**HR** (c)	**STMR** (b)
Option 1: Residue for monitoring defined as flonicamid only						
Apple/pear	N/S	2x <0.01; 4x 0.01; 4x 0.02; 2x 0.03; 0.045; 2x 0.08; 0.085	R_{ber}: 0.08, R_{max} 0.10	0.1	0.085	0.02
Peach	S	0.02; 3x 0.03; 0.04; 0.06; 0.08; 0.09; 0.18; 0.26	R_{ber}: 0.23, R_{max} 0.31	0.3	0.26	0.05
Potato	N/S	17x<0.01, 0.01		0.01*	0.01	0.01
Wheat	N/S	**Grain:** 14x <0.01;0.01; <0.02; 0.02; 0.04; 0.06	R_{ber}: 0.02, R_{max} 0.05	0.1	0.06	0.01
		Straw: 6x <0.02; 0.02; 2x 0.03; 2x 0.04; 2x 0.05. 0.08; 0.09; 0.11; 0.23; 0.39			0.39	0.03
Option 2: Residue for monitoring defined as sum flonicamid. TFNA. TFNG expressed as flonicamid						
Apple/pear	N/S	<0.03; 3x 0.03; 3x 0.04; 2x 0.044; 0.054; 0.064; 0.076; 0.115; 0.126; 0.15; 0.185	R_{ber}: 0.21, R_{max} 0.19	0.2	0.185	0.04
Peach	S	0.04; 3x 0.05; 0.06; 0.094; 0.10; 0.11; 0.208; 0.298	R_{ber}: 0.27, R_{max} 0.35	0.5	0.298	0.08
Potato	N/S	8x <0.03; 5x 0.03; 3x 0.044; 0.048; 0.056	R_{ber}: 0.09, R_{max} 0.06	0.1	0.056	0.03
Wheat	N/S	**Grain:** 0.038; 0.075; 0.084; 0.117; 0.130; 0.149; 0.203; 0.227; 0.267; 0.350; 0.466; 0.517; 0.521; 0.552; 0.570; 0.585; 0.738; 1.124	R_{ber}: 1.11, R_{max} 1.07	2.0	1.124	0.31
		Straw: 4x< 0.06; 0.105; 0.106; 0.132; 0.144; 0.150; 0.162; 0.178; 0.179; 0.196; 0.268; 0.407; 0.422; 0.474; 0.477			0.477	0.156

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01. 1 x 0.01. 6 x 0.02. 1 x 0.04. 1 x 0.08. 2 x 0.1. 2 x 0.15. 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

Consumer risk assessment

	NOT PEER REVIEWED
ADI	0.025 mg/kg per day
TMDI (European diet) (% ADI)	**TMDI using EFSA PRIMO Model** **- Option 1:** 63% ADI (WHO Cluster diet B) using conversion factors of 2.5, 1.6, 3.0 and 17.5 for apple, peach, potato and wheat **- Option 2:** 72% ADI (WHO Cluster diet B)
NEDI (% ADI)	-
Factors included in NEDI	-
ARfD	0.025 mg/kg per day
Acute exposure (% ARfD)	**IESTI using EFSA PRIMO Model** (% ARfD) **- Option 1:** Using MRL and conversion factors: Peach 114%, Wheat 101%, Apple 98%, Pear 91%, Potato 19% Using HR corrected by conversion factors: Peach 99%, Apple 83%, Pear 77%, Wheat 61%, Potato 19% **Option 2:** Using MRL: Peach 119%, Wheat 116%, Apple 78%, Pear 73%, Potato 62% Using HR: Apple 73%, Peach 71%, Pear 67%, wheat 64%, Potato 34%

Processing factors

Crop/processed crop	Number of studies	Transfer factor
Wheat: bread (whole meal)	4	0.28 – 0.86 (mean: 0.58)
Plum/Prune	1	2.5

* Calculated on the basis of distribution in the different portions. parts. or products as determined through balance studies.

Proposed MRLs

	Residues for Monitoring defined as	
Plant products	Flonicamid	Flonicamid+TFNA+TFNG
Apple/Pears	0.1	0.2
Peaches	0.3	0.5
Potatoes	0.01*	0.1
Wheat	0.1	2

Animal products	0.02* (residues defined as flonicamid+TFNA-AM)

Route of degradation (aerobic) in soil (Annex IIA. point 7.1.1.1.1)

Mineralization after 100 days	47-56.6 % after 30 d (4 soils)
Non-extractable residues after 100 days	29.6-43.3 % after 30 d (4 soils)
Relevant metabolites - name and/or code. % of applied (range and maximum)	TFNA : 12.2-36.4 % after 1-3 d TFNA-OH : 12.1-21.3 % after 2-7 d TFNG-AM : 7.8-10.2 % after 0.3-2 d TFNG : < 3.9 % TFNA-AM : 7.6 % after 7 d

Route of degradation in soil - Supplemental studies (Annex IIA. point 7.1.1.1.2)

Anaerobic degradation	No data provided. not required (April-July applications)
Soil photolysis	DT_{50} : 53 d (dark) and 22 d (continous artificial light) on dry soil TFNG-AM : 13.8 % (dark). 29.5 % (light) after 15 d Negligible role of photodegradation

Rate of degradation in soil (Annex IIA. point 7.1.1.2. Annex IIIA. point 9.1.1)

Method of calculation	1st order by linear regression. $R^2 > 0.94$
Laboratory studies (range or median. with n value. with r^2 value)	DT_{50lab} (20°C. aerobic): Flonicamid : 0.7-1.8 d (mean 1.1 d). 4 soils (pH 6.2-7.2) Flonicamid geometric mean 1 day TFNA : 0.29-0.46 d (mean 0.4 d). 3 soils (pH 5.7-6.8) TFNA-OH : 1.0-2.6 d (mean 1.6 d). 3 soils (pH 5.7-6.8) TFNG-AM : 0.2-1.0 (mean 0.5 d). 3 soils (pH 6.2-7.0) TFNG : 0.1-1.1 d (mean 0.5 d). 3 soils (pH 5.7-6.8) TFNA-AM : 1.0-2.6 d (mean 1.6 d). 3 soils (pH 6.2-7.0)
	DT_{90lab} (20°C. aerobic): Flonicamid : 2.3-6.0 d (mean 3.5 d) TFNA : 1.0-1.5 d (mean 1.3 d) TFNA-OH : 3.4-8.7 d (mean 5.4 d) TFNG-AM : 0.6-3.3 (mean 1.6 d) TFNG : 0.4-3.5 d (mean 1.5 d) TFNA-AM : 3.4-8.5 d (mean 5.2 d)
	DT_{50lab} (10°C. aerobic): Flonicamid : 2.4 d TFNA : 0.99 d TFNA-OH : 4.5 d TFNG-AM : 0.7 d TFNG : 0.3 d

	TFNA-AM : 4.8 d
	DT_{50lab} (20°C. anaerobic): No data. not required (April-July applications)
	degradation in the saturated zone:
Field studies (state location. range or median with n value)	DT_{50f}: : no data. not required
	DT_{90f}: : no data. not required
Soil accumulation and plateau concentration	No data. not required

Soil adsorption/desorption (Annex IIA. point 7.1.2)

K_f /K_{oc} K_d pH dependence (yes / no) (if yes type of dependence)	Flonicamid	Kd : 0.03-0.17 L/kg Kdoc : 2.5-8.7 L/kg (mean 5.9) 4 soils (pH 6.5-7.6)
	TFNA	Kd : < 0.02 L/kg Kdoc : < 3.0 L/kg (mean about 2.0) 4 soils (pH 5.7-7.2)
	TFNA-OH	Kd : < 0.06 L/kg Kdoc : < 4.4 L/kg (mean about 3.0) 4 soils (pH 5.7-7.2)
	TFNG-AM	Kd : 0.04-0.32 L/kg Kdoc : 5.5-13.2 L/kg (mean 9.2) 4 soils (pH 5.6-7.2)
	TFNG	Kd : < 0.03 L/kg Kdoc : < 4.0 L/kg (mean about 1.6) 4 soils (pH 5.7-7.2)
	TFNA-AM	Kd : 0.03-0.20 L/kg Kdoc : 2.8-12.1 L/kg (mean 6.2) 9 soils (pH 5.6-8.1)
	No pH dependence for flonicamid or its metabolites.	

Mobility in soil (Annex IIA. point 7.1.3. Annex IIIA. point 9.1.2)

Column leaching	No data provided. not required
Aged residues leaching	No data provided. not required
Lysimeter/ field leaching studies	No data provided

PEC (soil) (Annex IIIA. point 9.1.3)

Method of calculation	5 cm soil layer. BD 1.5 Flonicamid : max. DT_{50lab} 1.8 d TFNA : max. 36.4 %. max. DT_{50lab} 0.5 d. MR 0.83 TFNA-OH : max. 21.3 %. max. DT_{50lab} 2.6 d. MR 0.90

	TFNG-AM : max. 10.2 %. max. DT_{50lab} 1.0 d. MR 1.08 TFNG : max. 3.9 %. max. DT_{50lab} 1.1 d. MR 1.08 TFNA-AM : max. 7.6 %. max. DT_{50lab} 2.6 d. MR 0.83
Application rate	Single application at 80 g/ha (potatoes) or 70 g/ha (apples and cereals). Crop interception : 50 %.

PECsoil (µg/kg) for single application at 80 g/ha to potatoes

Day	Flonicamid		TFNA		TFNA-OH		TFNA-AM		TFNG		TFNG-AM	
	Act	TWA	Act	TWA	Act	TWA	Act	TWA	Act	TWA	Act	TWA
Initial	53.3	53.3	16.1	16.1	10.2	10.2	3.4	3.4	2.2	2.2	5.9	5.9
1	36.3	44.2	4.0	8.7	7.8	9.0	2.6	3.0	1.2	1.6	3.0	4.3
2	24.7	37.2	1.0	5.4	6.0	7.9	2.0	2.6	0.6	1.3	1.5	3.2
4	11.4	27.2	0.1	2.9	3.5	6.3	1.2	2.1	0.2	0.8	0.4	2.0
7	3.6	18.4	-	1.7	1.6	4.6	0.5	1.5	-	0.5	-	1.2
28	-	4.9	-	0.4	-	1.4	-	0.5	-	0.1	-	0.3
50	-	2.8	-	0.2	-	0.8	-	0.3	-	0.1	-	0.2
100	-	1.4	-	0.1	-	0.4	-	0.1	-	-	-	0.1

PECsoil (µg/kg) for single application at 70 g/ha to cereals and orchards

Day	Flonicamid		TFNA		TFNA-OH		TFNA-AM		TFNG		TFNG-AM	
	Act	TWA	Act	TWA	Act	TWA	Act	TWA	Act	TWA	Act	TWA
Initial	46.7	46.7	14.1	14.1	8.9	8.9	2.94	2.94	1.97	1.97	5.14	5.14
1	31.7	38.8	3.5	7.6	6.8	7.8	2.25	2.58	1.05	1.46	2.57	3.71
2	21.6	32.6	0.9	4.8	5.2	6.9	1.72	2.28	0.56	1.12	1.28	2.78
4	10.0	23.8	0.1	2.5	3.1	5.5	1.01	1.81	0.16	0.72	0.32	1.74
7	3.2	16.1	-	1.5	1.4	4.0	0.45	1.33	-	0.44	0.04	1.05
28	-	4.3	-	0.4	-	1.1	-	0.39	-	0.11	-	0.26
50	-	2.4	-	0.2	-	0.7	-	0.22	-	0.06	-	0.15
100	-	1.2	-	0.1	-	0.3	-	0.11	-	-	-	0.07

For potato. 50 % interception is thought to be realistic for the current intended conditions of use (well developed plants). In case of earlier application (early stage of leaf development) 15 % interception could be realistic and PECs would be increased by a factor of 1.7. Such a particular condition of use should be dealt with at MS level if relevant. However with regard to safety margins. impact on the terrestrial risk assessment is not expected.

Route and rate of degradation in water (Annex IIA. point 7.2.1)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 4 : flonicamid and TFNA are stable
	pH 7: flonicamid and TFNA are stable
	pH 9 : DT_{50} 204 d (25° C). 17.1 d (40° C). 9.0 d (50° C) (1st order. linear regression) TFNG-AM : 65.1 % after 20 d at 50° C TFNG : 85.7 % after 120 d at 50° C TFNA : stable
Photolytic degradation of active substance and relevant metabolites	pH 7 . 23° C : stable (dark). DT_{50} 267 d (continous artifical light). Negligible role of photodegradation (Φ = 0.000319)
Readily biodegradable (yes/no)	No
Degradation in water/sediment - DT_{50} water - DT_{90} water	30.3-37.3 d (1st order. linear regression. n=2) 100.5-123.8 d

- DT_{50} whole system - DT_{90} whole system	35.7-43.6 d (1st order) 118.7-144.8 d
Mineralization	15.6-59.1 % (136-145 d)
Non-extractable residues	38.4-75.4 % (136-145 d)

Distribution in water / sediment systems (active substance)	Max. 17.8-43.7 % after 3 d due to high sediment:water ratio (1:4) and to high OC content up to 10.2 % (DT_{50} 41-69 d)
Distribution in water / sediment systems (metabolites)	TFNA : max. 9.6 % in water after 30 d (apparent DT_{50} 60 d) and 9.2 % in sediment after 42 d (apparent DT_{50} 59 d). TFNA-OH : max. 12.5 % in water after 42 d (apparent DT_{50} 49 d) and < 2.2 % in sediment. TFNG : < 3.7 % in water and < 2.7 % in sediment. TFNA-AM : < 0.9 % in water and < 1.1 % in sediment.

PEC (surface water) (Annex IIIA. point 9.2.3)

Method of calculation	FOCUS-SW step 1 Mean DT_{50} flonicamid in water/sediment : 39.7 d Mean Koc flonicamid : 19 (notifier proposal. 5.9 should be used) FOCUS-SW step 2 Soil : mean DT_{50lab} (flonicamid/TFNA/TFNA-OH/TFNA-AM/TFNG/TFNG-AM) = 1.1 /0.4 /1.6 /1.6 /0.5 /0.5 Soil : Max. amounts of metabolites (TFNA/TFNA-OH/TFNA-AM/TFNG/TFNG-AM) = 36.4 /20.2 /6.9 /2.5 /9.6 (% of parent) Water/sed : mean DT_{50} whole system for both phases (flonicamid/TFNA/TFNA-OH/TFNA-AM/TFNG/TFNG-AM) = 39.7/ 69.3/ 69.3 / 69.3 / 69.3 / 69.3 (flonicamid : notifier proposal. 55 d should be used) Water : max. amounts of metabolites in whole system (TFNA/TFNA-OH/TFNA-AM/TFNG/TFNG-AM) = 17.9 /13.2 /1.1 /3.5 /1.0 (% of parent) Koc : mean values (flonicamid/TFNA/TFNA-OH/TFNA-AM/TFNG/TFNG-AM) = 19 /1.6 /3.0 /4.6 /1.7 /5.3 (flonicamid: notifier proposal. 5.9 should be used)
Application rate	Apples : 3 x 70 g/ha. 21 d interval. 70 % interception Potatoes : 2 x 80 g/ha. 21 d interval. 50 % interception Wheat : 2 x 70 g/ha. 21 d interval. 70 % interception
Main routes of entry	Step 1 Spray drift : 15.7 % at 3 m for apples. 2.76 % at 1 m for potatoes and wheat Run-off/drainage : 10 % Step 2 Spray drift : overall 90th percentile (11 % at 3 m for apples. 2.44 % at 1 m for potatoes and wheat) Run-off/drainage : 3 % of soil residue 4 DALA

PECsw (µg/L) for flonicamid - step 1 calculation

Day	Apples		Potatoes		Wheat	
	Actual	TWA	Actual	TWA	Actual	TWA
Initial	79.2		53.4		46.8	
1	77.6	78.4	52.5	53.0	45.9	46.3
2	76.2	77.7	51.6	52.5	45.1	45.9
4	73.6	76.3	49.8	51.6	43.6	45.1
7	69.9	74.3	47.3	50.3	41.3	44.0
14	61.8	70.1	41.8	47.2	36.6	41.4
21	54.7	66.1	37.0	44.7	32.4	39.1
28	48.4	62.4	32.7	42.2	28.6	36.9
42	37.9	55.9	25.6	37.8	22.4	33.1
50	33.0	52.7	22.3	35.6	19.5	31.1
100	13.7	37.3	9.3	25.2	8.1	22.1

PECsw (µg/L) for flonicamid for multiple applications (worst case) – step 2 calculation

Day after max	Apples (max. at 42 d) [1]		Potatoes (max. at 25 d) [1]		Wheat (max. at 25 d) [1]	
	Actual	TWA	Actual	TWA	Actual	TWA
0	5.53		1.32		1.04	
1	5.39	5.46	1.29	1.30	1.02	1.03
2	5.30	5.40	1.26	1.29	1.00	1.02
4	5.28	5.32	1.22	1.27	0.97	1.00
7	4.97	5.23	1.16	1.23	0.92	0.98
14	4.40	4.96	1.02	1.16	0.81	0.92
21	3.89	4.68	0.91	1.10	0.72	0.87
28	3.44	4.43	0.80	1.04	0.63	0.82
42	2.70	3.97	0.63	0.93	0.49	0.73
50	2.34	3.74	0.54	0.87	0.43	0.69
100	0.98	2.65	0.22	0.62	0.18	0.49

[1] time for the max. concentration starting from the first application

PECsw (µg/L) for metabolites for multiple applications to apples (worst case) – step 2 calculation

Day after max	TFNA		TFNA-OH		TFNA-AM		TFNG		TFNG-AM	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
0	0.94		0.79		0.076		0.24		0.068	
1	0.93	0.94	0.78	0.78	0.075	0.076	0.23	0.23	0.067	0.068
2	0.92	0.93	0.77	0.78	0.074	0.075	0.23	0.23	0.066	0.067
4	0.90	0.92	0.76	0.77	0.073	0.074	0.23	0.23	0.066	0.067
7	0.88	0.91	0.73	0.76	0.071	0.073	0.22	0.23	0.064	0.066
14	0.82	0.88	0.68	0.73	0.066	0.071	0.20	0.22	0.060	0.064
21	0.76	0.85	0.64	0.71	0.061	0.068	0.19	0.21	0.056	0.062
28	0.71	0.82	0.59	0.69	0.057	0.066	0.18	0.20	0.052	0.060
42	0.62	0.77	0.52	0.64	0.050	0.062	0.15	0.19	0.045	0.056
50	0.57	0.74	0.48	0.62	0.046	0.060	0.14	0.18	0.042	0.054
100	0.34	0.59	0.29	0.50	0.028	0.048	0.08	0.15	0.025	0.043

PEC (sediment)

Method of calculation	See PECsw
Application rate	See PECsw

PECsed (µg/kg) for flonicamid - step 1 calculation

Day	Apples		Potatoes		Wheat	
	Actual	TWA	Actual	TWA	Actual	TWA
Initial	12.9		9.8		8.6	
1	14.7	13.8	9.9	9.9	8.7	8.6
2	14.4	14.2	9.8	9.9	8.5	8.6
4	13.9	14.2	9.4	9.7	8.2	8.5
7	13.2	13.9	8.9	9.5	7.8	8.3
14	11.7	13.2	7.9	9.0	6.9	7.8
21	10.4	12.5	7.0	8.4	6.1	7.4
28	9.2	11.8	6.2	8.0	5.4	7.0
42	7.2	10.6	4.8	7.1	4.2	6.2
50	6.2	9.9	4.2	6.7	3.7	5.9
100	2.6	7.0	1.7	4.8	1.5	4.2

PECsed (µg/kg) for flonicamid for multiple applications (worst case) – step 2 calculation

Day after max	Apples (max. at 47 d)		Potatoes (max. at 26 d)		Wheat (max. at 26 d)	
	Actual	TWA	Actual	TWA	Actual	TWA
0	0.97		0.24		0.19	
1	0.96	0.97	0.24	0.24	0.19	0.19
2	0.94	0.96	0.23	0.24	0.18	0.19
4	0.91	0.94	0.22	0.23	0.18	0.18
7	0.86	0.92	0.21	0.23	0.17	0.18
14	0.76	0.86	0.19	0.21	0.15	0.17
21	0.67	0.81	0.17	0.20	0.13	0.16
28	0.60	0.77	0.15	0.19	0.11	0.15
42	0.47	0.69	0.11	0.17	0.09	0.13
50	0.40	0.65	0.10	0.16	0.08	0.12
100	0.17	0.46	0.04	0.11	0.03	0.09

PECsed (µg/kg) for metabolites for multiple applications to apples (worst case) – step 2 calculation

Day after max	TFNA		TFNA-OH		TFNA-AM		TFNG		TFNG-AM	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
0	0.014		0.023		0.003		0.004		0.004	
1	0.014	0.014	0.023	0.023	0.003	0.003	0.004	0.004	0.003	0.004
2	0.014	0.014	0.023	0.023	0.003	0.003	0.004	0.004	0.003	0.003
4	0.013	0.014	0.022	0.023	0.003	0.003	0.004	0.004	0.003	0.003
7	0.013	0.013	0.021	0.022	0.003	0.003	0.004	0.004	0.003	0.003
14	0.012	0.013	0.020	0.021	0.003	0.003	0.003	0.004	0.003	0.003
21	0.011	0.013	0.019	0.021	0.003	0.003	0.003	0.004	0.003	0.003
28	0.010	0.012	0.017	0.020	0.003	0.003	0.003	0.003	0.003	0.003
42	0.009	0.011	0.015	0.019	0.002	0.003	0.003	0.003	0.002	0.003
50	0.008	0.011	0.014	0.018	0.002	0.003	0.002	0.003	0.002	0.003
100	0.005	0.009	0.008	0.014	0.001	0.002	0.001	0.003	0.001	0.002

PEC (ground water) (Annex IIIA. point 9.2.1)

Method of calculation and type of study (*e.g.* modelling. monitoring. lysimeter)	FOCUS-PELMO Flonicamid : mean DT_{50lab} 1.1 d. mean Koc 1.6 (first rapporteur proposal. 5.9 should be used). 1/n 0.9 (default) Q10 2.2, Walker equation coefficient 0.7
Application rate	Apples : 3 x 70 g/ha. 21 d interval. interception 65-80 % Potatoes : 2 x 80 g/ha. 21 d interval. interception 15-50 % Wheat : 2 x 70 g/ha. 21 d interval. interception 70-90 %

$PEC_{(gw)}$

Maximum concentration	Value not produced by FOCUS shells. not required.
Average annual concentration	PECgw < 0.001 µg/L for flonicamid (all scenarios) No reliable PECgw available for metabolites. Concentrations are not expected to exceed those of flonicamid (lower amounts in soil. similar properties).

Fate and behaviour in air (Annex IIA. point 7.2.2. Annex III. point 9.3)

Direct photolysis in air	Not available. not required
Quantum yield of direct phototransformation	Not applicable
Photochemical oxidative degradation in air	DT_{50} ..13.7 d (12 h day) for K_{OH} 0.779 x 10^{-12} cm^3 $molecule^{-1}$ sec^{-1} and [OH] 1.5 x 10^6 radicals per cm^3
Volatilization	from plant surfaces: no data provided
	from soil: no data provided

PEC (air)

Method of calculation	Expert judgement based on physico chemical properties

$PEC_{(a)}$

Maximum concentration	Flonicamid has a low vapour pressure (9.43 x 10^{-7} Pa at 20° C) and a low Henry law constant (4.2 x 10^{-8} Pa m^3 $mole^{-1}$). Accordingly negligible concentrations are expected in air despite slow photo-oxidation in air.

Definition of the Residue (Annex IIA. point 7.3)

Relevant to the environment	Soil : flonicamid. TFNA. TFNA-OH. TFNG-AM. TFNG. TFNA-AM Residue for monitoring : flonicamid Groundwater : flonicamid. TFNA. TFNA-OH. TFNG-AM. TFNG. TFNA-AM Residue for monitoring : flonicamid

Surface water : flonicamid. TFNA. TFNA-OH. (TFNG-AM originating from soil) Residue for monitoring : flonicamid
Sediment : flonicamid

Air : flonicamid

Monitoring data. if available (Annex IIA. point 7.4)

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

Classification and proposed labelling (Annex IIA. point 10)

with regard to fate and behaviour data	Candidate for R53

Effects on terrestrial vertebrates (Annex IIA. point 8.1. Annex IIIA. points 10.1 and 10.3)

Toxicity to mammals	Short-term LD50 = 884 mg a.s./kg bw Long-term NOEL (teratogenicity) = 25 mg a.s./kg bw/d
Acute toxicity to birds	LD50 (quail. boths sexes) > 2000 mg a.s./kg bw LD50 (duck. male) = 2621 mg a.s./kg bw LD50 (duck. female) = 1591 mg a.s./kg bw
Dietary toxicity to birds	LD50 (quail) > 411 mg a.s./kg bw/d LD50 (duck) > 301.8 mg a.s./kg bw/d
Reproductive toxicity to birds	NOEL (quail) = 90 mg a.s./kg bw/d NOEL (duck) = 59 mg a.s./kg bw/d

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA. points 10.1 and 10.3)

Exposure assessment according to SANCO/4145/2000 (25.09.02)

Birds

Application rate (kg as/ha)	Crop	Category *(feed item)*	Time-scale	TER	Annex VI Trigger
0.08	potatoes	medium herbivorous bird insectivorous bird	acute	251 368	10
0.07	wheat. apples. pears. peaches	insectivorous bird	acute	420	10
0.08	potatoes	medium herbivorous bird insectivorous bird	short-term	> 103 > 125	10
0.07	wheat. apples. pears. peaches	insectivorous bird	short-term	> 143	10
0.08	potatoes	medium herbivorous bird insectivorous bird	long-term	38 24	5
0.07	wheat. apples. pears. peaches	insectivorous bird	long-term	28	5

Small mammals: Tier 1

Application rate (kg as/ha)	Crop	Category *(feed item)*	Time-scale	TER	Annex VI Trigger
0.08	potatoes	medium herbivorous mammal	acute	378	10
0.07	wheat	insectivorous mammal	acute	1433	10
0.07	apples. pears	small herbivorous mammal	acute	77	10
0.07	peaches	small herbivorous mammal	acute	89	10
0.08	potatoes	medium herbivorous mammal	long-term	42.9	5
0.07	wheat	insectivorous mammal	long-term	111	5
0.07	apples. pears	small herbivorous	long-term	8.23	5

		mammal			
0.07	peaches	small herbivorous mammal	long-term	8.60	5

Toxicity data for aquatic species (Annex IIA. point 8.2. Annex IIIA. point 10.2)

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Laboratory tests				
O. mykiss	a.s.	acute	LC50-96 h	> 100 mg a.s./L
O. mykiss	IKI-220 50%WG	acute	LC50-96 h	> 51 mg a.s./L
L. macrochirus	a.s.	acute	LC50-96 h	> 100 mg a.s./L
P. promelas	a.s.	chronic	NOEC-33 d	10 mg a.s./L
D. magna	a.s.	acute	EC50-48 h	> 100 mg a.s./L
D. magna	IKI-220 50%WG	acute	EC50-48 h	> 51 mg a.s./L
D. magna	a.s.	chronic	NOEC-21 d	3.1 mg a.s./L
Ps. subcapitata	a.s.		EbC50-72 h ErC50-72 h	> 100 mg a.s./L > 100 mg a.s./L
Ps. subcapitata	IKI-220 50%WG		EbC50-72 h ErC50-72 h	43 mg a.s./L > 51 mg a.s./L
L. gibba	a.s.		EC50 biomass and growth-7 d	119 mg a.s./L
C. riparius	a.s.	acute	LC50-48 h	> 200 mg a.s./L
C. riparius	a.s.	chronic	NOEC-28 d	25 mg a.s./L
O. mykiss	TFNA	acute	LC50-96 h	> 100 mg a.s./L
D. magna		acute	EC50-48 h	> 100 mg a.s./L
Ps. subcapitata			EbC50-72 h ErC50-72 h	> 100 mg a.s./L > 100 mg a.s./L
O. mykiss	TFNA-OH	acute	LC50-96 h	> 100 mg a.s./L
D. magna		acute	EC50-48 h	> 100 mg a.s./L
Ps. subcapitata			EbC50-72 h ErC50-72 h	29 mg a.s./L > 100 mg a.s./L
O. mykiss	TFNA-AM	acute	LC50-96 h	> 100 mg a.s./L
D. magna		acute	EC50-48 h	> 100 mg a.s./L
Ps. subcapitata			EbC50-72 h ErC50-72 h	> 100 mg a.s./L > 100 mg a.s./L
O. mykiss	TFNG-AM	acute	LC50-96 h	> 100 mg a.s./L
D. magna		acute	EC50-48 h	> 100 mg a.s./L
Ps. subcapitata			EbC50-72 h ErC50-72 h	> 100 mg a.s./L > 100 mg a.s./L

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA. point 10.2)

Active substance (exposure assessment according to FOCUS-Step 1)

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
0.08	apples (worst case)	fish	acute	3	> 643	100
		fish	chronic		126	10

		aquatic invertebrates	acute		> 643	100
		aquatic invertebrates	chronic		39	10
		algae			542	10
		aquatic plants			> 1501	10
		sed^{t} dwell^{ng} org^{ms}	chronic		315	10

Metabolites (exposure assessment according to FOCUS-Step 2)

Substance	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
TFNA	apples (worst case)	fish	acute	3	> 105 708	100
		aquatic invertebrates	acute		> 105 708	100
		algae			> 105 708	10
TFNA-OH	apples (worst case)	fish	acute	3	> 126 582	100
		aquatic invertebrates	acute		> 126 582	100
		algae			36 709	10
TFNA-AM	apples (worst case)	fish	acute	3	> 1.3 x 10^6	100
		aquatic invertebrates	acute		> 1.3 x 10^6	100
		algae			> 1.3 x 10^6	10
TFNG-AM	apples (worst case)	fish	acute	3	> 1.47 x 10^6	100
		aquatic invertebrates	acute		> 1.47 x 10^6	100
		algae			> 1.47 x 10^6	10

Bioconcentration

Bioconcentration factor (BCF)	logPow = 0.3 (i.e.. < 3)
Annex VI Trigger:for the bioconcentration factor	
Clearance time (CT_{50}) (CT_{90})	
Level of residues (%) in organisms after the 14 day depuration phase	

Effects on honeybees (Annex IIA. point 8.3.1. Annex IIIA. point 10.4)

Acute oral toxicity	> 104.3 mg IKI-220 50% WG (TEPPEKI) / bee *i.e.*. > 53.3 mg a.s./bee
Acute contact toxicity	> 100.0 mg IKI-220 50% WG (TEPPEKI) / bee *i.e.*. > 51.1 mg a.s./bee

Hazard quotients for honey bees (Annex IIIA. point 10.4)

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.08	all crops	oral contact	< 1.5 < 1.6	50 50

Field or semi-field tests: Six tunnel tests were performed. Test item: TEPEKI (0.07-0.14 kg a.s./ha). One test with winter wheat. two tests with white mustard. three tests with oil seed rape. Only slight and transient effects were observed in some tests.

Effects on other arthropod species (Annex IIA. point 8.3.2. Annex IIIA. point 10.5)

Laboratory tests:

Species	Stage	Test Substance	Dose (g a.s./ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests						
A. rhopalosiphi (standard test)	adults	IKI-220 50% WG	80 210	mortality	22.2% 55.5%	30%
T. pyri (standard test)	protonymphs		80 210	mortality	100% 100%	30%
C. 7-punctata (standard test)	larvae		80 210	mortality	30% 30%	30%

Tier-1 risk assessment for flonicamid:

Test species	Toxicity endpoint	Lethal effect	Crop	Application rate in-field	HQ in-field
A. rhopalosiphi	LR50 > 80 g a.s./ha	22.2%	Potatoes	80	< 1
T. pyri	LR50 < 80 g a.s./ha	100	Potatoes	80	> 1
A. rhopalosiphi	LR50 > 80 g a.s./ha	22.2%	Wheat	70	< 0.88
T. pyri	LR50 < 80 g a.s./ha	100	Wheat	70	> 0.88
A. rhopalosiphi	LR50 > 80 g a.s./ha	22.2%	Apples/pears	70	< 0.88

Test species	Toxicity endpoint	Lethal effect	Crop	Application rate in-field	HQ in-field
T. pyri	LR50 < 80 g a.s./ha	100	Apples/pears	70	> 0.88
A. rhopalosiphi	LR50 > 80 g a.s./ha	22.2%	Peaches	70	< 0.88
T. pyri	LR50 < 80 g a.s./ha	100	Peaches	70	> 0.88

Tier 2 studies:

Species	Stage	Test Substance	Dose (g a.s./ha)	Endpoint	Effect	Annex VI Trigger
Extended laboratory tests						
A. rhopalosiphi (ext[d] test)	adults		85	mortality reproduction	4.4% 9.5% *	30%
T. pyri (ext[d] test)	protonymphs		85	mortality reproduction	23.3% 5.5% *	30%
C. 7-punctata (ext[d] test)	larvae		85	mortality reproduction	6.1% 14.3%	30%
C. carnea (ext[d] test)	larvae		85	mortality reproduction	18.8% - 18.5% *	30%
P. cupreus (standard test)	adults		45	mortality food consumption	3.3% - 0.8% *	30%
E. balteatus (ext[d] test)	larvae		85	mortality reproduction	2.3% 30.2%	30%
O. laevigatus (lab test)	2nd stage nymph		161 (dry residues)	mortality reproduction	22% 11%	30%
Field or semi-field tests: no data.						

* reduction.

Effects on earthworms (Annex IIA. point 8.4. Annex IIIA. point 10.6)

Acute toxicity	flonicamid > 1000 mg a.s./kg soil TFNA > 100 mg a.s./kg soil TFNA-OH > 100 mg a.s./kg soil TFNG-AM > 100 mg a.s./kg soil TFNA-AM > 100 mg a.s./kg soil
Reproductive toxicity	not required

Toxicity/exposure ratios for earthworms (Annex IIIA. point 10.6)

Substance	Crop	Time-scale	TER	Annex VI Trigger
flonicamid [0.08 kg a.s./ha]	all crops	acute	> 1876	10
TFNA		acute	> 6211	10
TFNA-OH		acute	> 9804	10

TFNG-AM		acute	> 16 950	10
TFNA-AM		acute	> 29 411	10

Effects on soil micro-organisms (Annex IIA. point 8.5. Annex IIIA. point 10.7)

Nitrogen transformation	0.105 kg a.s./ha: no effect > 25%
Carbon mineralization	0.105 kg a.s./ha: no effect > 25%

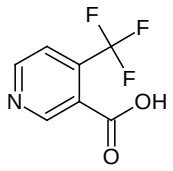
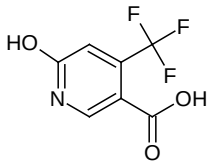
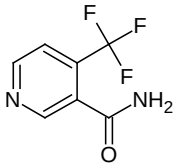
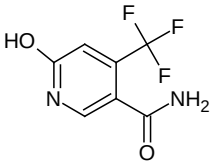
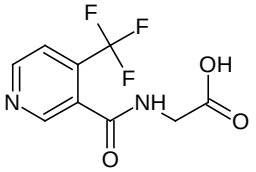
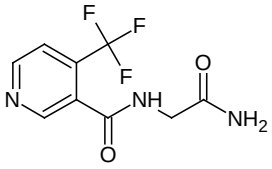
Effects on terrestrial plants (Annex IIA 8.6; Annex IIIA 10.8)

Foliar treatment	Eleven species. No effect in a screening test
Soil treatment	Seventeen species. No effect in a screening test

Classification and proposed labelling (Annex IIA. point 10)

with regard to ecotoxicological data	not classified

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name*	Structural formula*
TFNA	4-(trifluoromethyl)pyridine-3-carboxylic acid or 4-trifluoromethylnicotinic acid	
TFNA-OH	6-hydroxy-4-(trifluoromethyl)pyridine-3-carboxylic acid or 6-hydroxy-4-trifluoromethylnicotinic acid	
TFNA-AM	4-(trifluoromethyl)pyridine-3-carboxamide or 4-trifluoromethylnicotinamide	
OH-TFNA-AM	6-hydroxy-4-(trifluoromethyl)pyridine-3-carboxamide or 6-hydroxy-4-trifluoromethylnicotinamide	
TFNG	*N*-{[4-(trifluoromethyl)pyridin-3-yl]carbonyl}glycine or *N*-(4-trifluoromethylnicotinoyl)glycine	
TFNG-AM	*N*-(2-amino-2-oxoethyl)-4-(trifluoromethyl)pyridine-3-carboxamide or *N*-(4-trifluoromethylnicotinoyl)glycinamide	

* ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

ABBREVIATIONS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HR	hazard rate
IESTI	international estimated short term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
kg	kilogram
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mg	milligram
mN	milli-Newton
MRL	maximum residue limit or level

MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
pH	pH-value
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PELMO	Pesticides leaching model
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
TRR	Total radioactive residues
UDS	unscheduled DNA synthesis
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year