CONCLUSION ON PESTICIDE PEER REVIEW

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

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SUMMARY

Proquinazid is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[3] The United Kingdom received an application from DuPont de Nemours 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 The United Kingdom made the report of its initial evaluation of the dossier on proquinazid, hereafter referred to as the Draft Assessment Report (DAR), available on 14 March 2006.

The peer review was initiated on 9 June 2006 by distributing the DAR for consultation of the Member States and the applicant. Subsequently, the comments received on the DAR were examined by the rapporteur Member State in the reporting table. This table was evaluated by EFSA to identify the remaining issues. The identified 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 April – May 2009.

A final discussion of the outcome of the experts' discussions took place during a written procedure with the Member States in July 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 fungicide as proposed by the applicant which comprise foliar spraying to cereals and grapes against powdery mildew. Full details of the GAPs can be found in the list of end points in Appendix A to this report.

The representative formulated product for the evaluation was 'Proquinazid 200 g/L EC', an emulsifiable concentrate (EC), containing 200 g/L proquinazid, registered under different trade names in the EU.

There is no agreed technical specification at the moment.

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1 On request from the European Commission, Question No EFSA-Q-2009-00320, issued on 13 October 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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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. Adequate methods are available to monitor all compounds given in the respective residue definition in food/feed of plant origin and environmental matrices. However, if MRLs will be set in food of animal origin according to the proposed residue definition for monitoring, an analytical method for the determination of the compounds in the residue definition will be required.

In mammals, proquinazid is of low acute toxicity to rats following oral, dermal or inhalation exposure; it is not a skin or eye irritant nor a skin sensitiser. The relevant short term toxicity NOAELs are 2 mg/kg bw/day in rat (based on altered thyroid homeostasis and associated follicular cell hypertrophy) and <15 mg/kg bw/day in the dog (increased incidence of clear ocular discharge). Proquinazid did not show any genotoxic potential. The relevant NOAEL for long term toxicity is 1.2 mg/kg bw/day from a rat study, based on thyroid and hepatic hyperplasia. Proquinazid was proposed for classification as **R40 "Limited evidence of a carcinogenic effect"** based on increased incidence of hepatocellular adenomas in rats (equivocal evidence in mice) and also an increased incidence of intestinal-type cholangiocarcinomas in rats. Both tumours were considered of limited relevance for human risk assessment. Proquinazid did not cause substance-related effects on reproductive parameters or organs in adult rats. The parental and reproductive NOAELs are 2 mg/kg bw/day and 35 mg/kg bw/day respectively. The offspring NOAEL is 11 mg/kg bw/day based on reduced litter weight. Proquinazid is not a developmental toxicant: the maternal and developmental NOAELs are 30 mg/kg bw/day (rat) and 2.5 mg/kg bw/day (rabbit), respectively. Proquinazid is not neurotoxic. The Acceptable Daily Intake (ADI) is 0.01 mg/kg bw/day based on the NOAEL from the 2-year study in rat, with a safety factor of 100; the Acute Reference Dose (ARfD) is 0.2 mg/kg bw (from the 90-day oral study in dog, SF 100); the Acceptable Operator Exposure Level (AOEL) is 0.02 mg/kg bw/day based on the NOAEL of 2 mg/kg bw/day from the 90-day study in rats, SF 100. The operator exposure to proquinazid is below the AOEL even without PPE (for the German model only), as well as for workers and bystanders.

Metabolism of proquinazid was investigated in grapes and in wheat under outdoor field conditions. Based on the available data, the main metabolic reactions in the metabolism of proquinazid in wheat plants and grapes could be established. The significant residues in the various wheat fractions were proquinazid and the metabolite IN-MW977[5] that was a major metabolite. In/on grape berries, proquinazid was only slowly metabolised to form minor amounts of IN-MM671[6] and IN-MM991[7]. Thus, the overall picture of metabolism was found to be slightly different in wheat and grapes. To confirm the identity of a significant unextractable fraction as lignin, a metabolism study in apples was evaluated in an addendum but not peer reviewed.

The proposed residue definition for consumer risk assessment for cereals and grapes is proquinazid and metabolite IN-MW977. Since the toxicological reference values of proquinazid can be applied to metabolite IN-MW977, residues of proquinazid and metabolite IN-MW977 should be expressed as proquinazid.

The proposed residue definition for plant products for enforcement monitoring for cereals and grapes is proquinazid alone. A conversion factor of 2 was established for cereals and of 1 for grapes as IN-MW977 was not formed in grapes.

A sufficient number of supervised residue trials are available in Northern and Southern Europe to support the representative uses on cereals and on grapes. The residue levels obtained in both Northern Europe and Southern Europe were similar. MRLs could be proposed for the different cereal crops

[5] IN-MW977: 2-{[(2*RS*)-2-hydroxypropyl]oxy}-6-iodo-3-propylquinazolin-4(3*H*)-one
[6] IN-MM671: 2-propoxy-3-propylquinazolin-4(3*H*)-one
[7] IN-MM991: 3-propylquinazoline-2,4(1*H*,3*H*)-dione

barley, rye wheat, oats, triticale and for grapes. The trials are supported by valid storage stability data and validated analytical methods.

In a rotational crop study significant total residues were detected in feed items, e.g. soybean straw and wheat forage and straw, while residues were <0.01 mg/kg in crop parts for human consumption. The experts in PRAPeR 70 considered in particular that metabolite IN-MM671 is very persistent in soil and that it may accumulate in soil. Further assessment by the RMS was required, but the evaluation provided is not peer reviewed. Therefore a final peer reviewed conclusion on whether significant amounts of metabolites may be expected in succeeding crops (mainly feed items) could not be drawn.

The metabolism and distribution of proquinazid was investigated in goats and in hen. Exposure to goats is significant. It was agreed that the following residue definition in animal matrices should be proposed for risk assessment: Sum of proquinazid and metabolites IN-MU210[8] and IN-MW977 expressed as proquinazid. It was further agreed that for monitoring, the following residue definition in animal matrices should be proposed: Sum of proquinazid and metabolite IN-MU210, expressed as proquinazid. Residues are not expected to exceed 0.01 mg/kg in animal products, considering the animal intake from the notified representative uses, however risk managers may consider to set MRLs for a fat-soluble residue in food of animal origin on the LOQ of the analytical method for monitoring.

In a consumer risk assessment it could be demonstrated that chronic and acute dietary intake of a range of consumer groups is well below the toxicological reference values ADI and ARfD, respectively.

Proquinazid exhibits moderate to high persistence in soil under aerobic conditions. The only major metabolite in the laboratory studies was IN-MM671. This metabolite is highly persistent in soil under aerobic conditions in the study performed with the parent compound and medium persistent in soil when applied as parent. Another metabolite, IN-MM991 was observed in one of the soils at levels above 5 % AR in two consecutive sampling dates. This metabolite is moderately persistent in soil. Metabolite IN-MM986[9] was also observed as a minor metabolite in soil and is moderately persistent. A water/sediment study under dark anaerobic conditions was provided as a surrogate of the soil anaerobic study. Proquinazid exhibits medium persistence in this study. The same metabolites identified under aerobic conditions were found.

Degradation of proquinazid was significantly enhanced by the irradiation of a light source simulating midday June sunlight in Phoenix, Arizona. Metabolite IN-MM671 was the main metabolite.

Dissipation of proquinazid was investigated in four field dissipation studies in a total of eight European sites (2 in UK, 2 in Northern France, 2 in Southern France, 1 in Italy, 1 in Germany). All field dissipation trials were performed on bare soil, therefore the contribution of photolysis to a certain extent may not be excluded. The metabolites IN-MM671, IN-MM991 and IN-MM986 appeared at levels above 10 % AR at various sampling points in the radiolabelled study. In non radiolabelled trials, only IN-MM671 and IN-MM986 were found consistently above 10 % of the applied amount. In these trials, proquinazid was low to medium persistent in soil, IN-MM671 was moderately to very highly persistent in soil, IN-MM986 was moderately to medium persistent and IN-MM991 moderately persistent to highly persistent.

According the results of the batch adsorption/desorption studies proquinazid may be considered immobile in soil, IN-MM671 slightly mobile, IN-MM991 medium to highly mobile and IN-MM986 slightly to low mobile in soil.

[8] IN-MU210: 3-[(6-iodo-4-oxo-3-propyl-3,4-dihydroquinazolin-2-yl)oxy]propanoic acid
[9] IN-MM986: 6-iodo-3-propylquinazoline-2,4(1*H*,3*H*)-dione

Proquinazid and all the metabolites investigated were stable to hydrolysis (pH 4, 7 and 9). In the aqueous photolysis study proquinazid is rapidly photolysed (DT50 < 1 h). Major photolysis metabolites identified were IN-MM671, IN-MM991, IN-MM986 and IN-MT884[10].

According to the available study, proquinazid is not readily biodegradable.

In water / sediment systems, proquinazid partitioned rapidly into the sediment (DissT50 < 1 d). However, it is moderately to highly persistent in the total system. The only metabolite identified was IN-MM671, which is very highly persistent in both systems. However this metabolite is strongly absorbed to the sediment and only amounts up to 6 % AR (after 30 d) are found in the water phase.

PECSW were calculated by the applicant following FOCUS SW scheme.

Potential groundwater contamination by proquinazid and its main soil metabolites was addressed with FOCUS GW PELMO 3.3.2. The concentrations of proquinazid and the metabolites IN-MM671, IN-MM991 and IN-MM986 were < 0.001 μg / L for all the uses and scenarios simulated.

No atmospheric long range transport is expected for proquinazid because the calculated half-life for photochemical oxidative degradation in the atmosphere was calculated to be 4 h.

Tier I assessment provided TER values above the Annex VI trigger values for the acute and short-term risk to birds. The long-term TER values were above the Annex VI trigger value for insectivorous and herbivorous birds for the use in cereals, whereas the TER for insectivorous birds for the use in vine failed to meet the trigger. The potential long-term risk for insectivorous birds in vine was refined by considering Yellowhammer (Emberiza citronella) and Cirl bunting (Emberiza cirlus), and their respective diets, as focal species. A mean of the 'Residue unit dose' for small and large insects was used and the resulting TERlt for insectivorous birds was above the trigger values. The acute and long-term risk to mammals was considered to be low.

The most likely exposure route for the metabolites would be through ingestion of contaminated earthworms or fish. Just the parent proquinazid and the metabolite IN-MM671 were considered for the assessment of secondary poisoning of earthworm- and fish-eating birds and mammals. Risk to earthworm- and fish-eating birds and mammals for cereals, was considered to be low. The high risk identified for the fish-eating birds for vine was refined using the 21 days TWA PECsw from FOCUSsw step 3. With the available information the risk for the earthworm-eating birds following the use of proquinazid in vines could not be considered as low. The risk from uptake of contaminated water was considered to be low.

Proquinazid was considered to be very toxic to aquatic organisms. The acute risk to aquatic organisms was addressed at FOCUSsw step 2, without risk mitigation for the use in cereals. Risk mitigation measures equivalent to a 5 m non-spray buffer zone were needed to address the acute risk to aquatic organism from the use in vines. For the long-term risk, TER values were below the Annex VI trigger values. FOCUS Step 4 calculations showed that non-spray buffer zones of 3 and 16 m for the use of proquinazid in cereals and vine respectively are necessary to protect the aquatic environment in the worst case scenarios. The risk of the relevant metabolites (IN-MM671, IN-MM986, IN-MM991) to aquatic organisms was considered to be low.

The risk to bees, non-target arthropods, earthworms, soil non-target micro-organisms and biological methods of sewage treatment was assessed as low.

[10] IN-MT884: 4-(2-carboxyethyl)-6-oxo-2-propoxy-1-propyl-1,6-dihydropyrimidine-5-carboxylic acid

KEY WORDS

Proquinazid, peer review, risk assessment, pesticide, fungicide

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BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC The United Kingdom received an application from DuPont de Nemours for inclusion of the active substance proquinazid 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 The United Kingdom submitted the report of its initial evaluation of the dossier on proquinazid, hereafter referred to as the Draft Assessment Report (DAR) (The United Kingdom, 2006), to the EFSA on 14 March 2006. The DAR was distributed for consultation to the Member States and the applicant on 9 June 2006.

The comments received on the DAR were evaluated by the rapporteur Member State in the reporting table. This table was evaluated by EFSA to identify the remaining issues. The identified 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 April – May 2009. The reports of these meetings have been made available to the Member States electronically.

A final consultation on the outcome of the experts' discussions took place during a written procedure with the Member States in August 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 Health, 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 (EFSA, 2009) 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 (revision 1-1; 31 October 2008),

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation,
- the evaluation table (revision 2-1; 30 September 2009)

Given the importance of the DAR including its addendum (compiled version of July 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

Proquinazid is the ISO common name for 6-iodo-2-propoxy-3-propylquinazolin-4(3*H*)-one (IUPAC).

Proquinazid belongs to a new group of fungicides, the quinazolinones. It acts by blocking secondary appressorial development in powdery mildew; it does not inhibit germ tube growth. The precise mode of action however has not been determined. It is used for the control of powdery mildew in cereals and grapes.

The representative formulated product for the evaluation was 'Proquinazid 200 g/L EC', an emulsifiable concentrate (EC), containing 200 g/L proquinazid, registered under different trade names in the EU.

The representative uses evaluated comprise foliar spraying with hydraulic sprayer with or without air assistance against:

- powdery mildew (*Blumeria graminis*) in winter and spring wheat and winter and spring barley, oats, triticale, winter rye, from growth stage BBCH 25 up to growth stage of BBCH 65 for wheat and up to BBCH 49 for the other cereals, in all EU countries, up to a maximum of two applications at a maximum individual application rate per spray of 50 g a.s./ha, with an interval of 14 days between applications, and

- powdery mildew (*Uncinula necator*) in grapes, from growth stage of BBCH 13 up to 28 DBH, in all EU countries, up to a maximum of four applications at a maximum individual application rate per spray of 75 g a.s./ha, with an interval of 14 days between applications.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of proquinazid technical could not be concluded on. The new specification was discussed at the PRAPeR 66 meeting and the experts could not come to a conclusion on the minimum purity and the maximum limits of the three impurities. As a consequence, a new data gap was proposed for a revised specification or a justification concerning the maximum limits of the above mentioned impurities and the minimum purity. There is no FAO specification available.

Besides the specification, 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 proquinazid or the respective formulations.

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

Adequate analytical methods are available for the determination of proquinazid in the technical material (HPLC-UV) and in the representative formulation (GC-FID) as well as for the determination of the respective impurities in the technical material (HPLC-UV, GC-FID).

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.

Residues of proquinazid in food of plant origin can be monitored by the modified multi-residue enforcement method DFG S19, with GC-MS with LOQs of 0.01 mg/kg for apple, grape and wheat grain, 0.02 mg/kg for oilseed rape and 0.1 mg/kg for wheat straw.

Residues of proquinazid in food of animal origin can be monitored by the modified multi-residue enforcement method DFG S19, with GC-MS with a LOQ of 0.02 mg/kg for meat. It should also be mentioned, that for food/feed of animal origin the residue definition proposed is sum of proquinazid and metabolite IN-MU210[11], expressed as proquinazid. As a consequence, if MRLs will be set in food of animal origin according to the proposed residue definition for monitoring, an analytical method for the determination of the compounds in the residue definition will be required.

An adequate GC-MS method is available to monitor residues of proquinazid and the metabolites IN-MM986[12], IN-MM671[13] and IN-MM991[14] in soil with LOQs of 0.005 mg/kg for each compound.

Proquinazid and also the metabolites IN-MM986, IN-MM671 and IN-MM991 can be determined in surface, ground and drinking water by GC-MS with LOQs of 0.1 µg/L for each compound.

Residues of proquinazid in air can be monitored by GC-MS with a LOQ of 0.8 µg/m^3.

Analytical methods for the determination of residues in body fluids and tissues are not required as proquinazid is not classified as toxic or highly toxic.

2. Mammalian toxicity

Proquinazid mammalian toxicity was discussed during the PRAPeR meeting 69 held in Parma in May 2009.

The majority of toxicological studies summarised in the DAR were conducted with proquinazid manufactured according to the old production process (with the exception of the acute studies which were conducted with proquinazid manufactured according to the current production process). The two different processes result in different purity and impurity profiles of technical materials, therefore bridging studies (90-day feeding study in rats and two genotoxicity assays) were conducted to compare their toxicity. In addition, a multigeneration study in rats with the current batch was also submitted. It was concluded that the proposed technical specification has been adequately supported by the submitted toxicity studies.

During the meeting the impurities in the new specification presented in the addendum to the DAR were discussed. One impurity was increased from 10 to 15 g/kg; two new impurities were present in the proposed specification at 2 g/kg. One of them is structurally very similar to proquinazid and was expected to have a similar metabolic and toxicological profile, both quantitatively and qualitatively; no concerns were identified by experts. The second one was considered of no concern as the levels were lower in the new proposed specification than in batch KQ926-45 where it had been fully tested. All other impurities were present at <1% apart from one present at max. 2% and toxicologically well known, and a second one, which was tested in an old batch up to 13.6 g/kg and is a metabolite of proquinazid in rats. No concerns were identified by the toxicological experts with respect to the technical specification proposed by the applicant (although it is noted that the technical specification was not agreed by the chemistry experts at PRAPeR meeting 66).

2.1. Absorption, distribution, excretion and metabolism (toxicokinetics)

Proquinazid is extensively absorbed after single oral low dose administration (86-89% within 48h, based on a bile-cannulation experiment) with the peak plasma concentration reached after 4-8h (low dose) or 6-10h (high dose of 20 mg/kg bw). Proquinazid and metabolites are widely distributed in the

[11] IN-MU210: 3-[(6-iodo-4-oxo-3-propyl-3,4-dihydroquinazolin-2-yl)oxy]propanoic acid
[12] IN-MM986: 6-iodo-3-propylquinazoline-2,4(1*H*,3*H*)-dione
[13] IN-MM671: 2-propoxy-3-propylquinazolin-4(3*H*)-one
[14] IN-MM991: 3-propylquinazoline-2,4(1*H*,3*H*)-dione

body (highest tissue levels in adrenals, liver, kidneys, fat). Excretion is rapid and extensive, equally important via urine and faeces, with biliary excretion accounting for nearly all of the faecal excretion. There is no evidence of significant bioaccumulation. Proquinazid is extensively metabolised, mainly through phenyl ring hydroxylation and hydroxylation at the propyl and propoxy side chains, as well as some hydrolysis of side chains.

2.2. Acute toxicity

Proquinazid is of low acute toxicity to rats following oral, dermal or inhalation exposure (oral LD50 4846 mg/kg bw, dermal LD50 > 5000 mg/kg bw, LC50 > 5.2 mg/l air /4h). It is not a skin or eye irritant nor a skin sensitiser.

2.3. Short-term toxicity

The administration of proquinazid in rats caused altered thyroid homeostasis and associated reversible follicular cell hypertrophy, decreased body weight and reversible liver hypertrophy. The toxicity of proquinazid technical produced with the old and the new process is mostly equivalent with regard to the thyroid effects; a reduction in white blood cells of uncertain toxicological relevance occurred in female rats administered with proquinazid manufactured by the new process.

In dogs, reduced body weight gain was the main adverse effect. Dogs showed an increased incidence of ocular discharge following both dietary and capsule administration. During PRAPeR 69 the Member States discussed the relevant NOAEL of the 1-year dog study, taking into account the occurrence of this effect and its toxicological relevance. There were ocular findings in both the 90-day and 1-year studies in dogs. No clear conclusion as to whether these findings were a systemic or a local effect could be made by the RMS. In the 1-year study there was a slight increase in incidence of ocular discharge at 15 mg/kg bw/day in females and on this basis the RMS proposed a NOAEL of <15 mg/kg bw/day for females. A NOAEL of 15 mg/kg bw/day for males was proposed considering the reduced body weight gain at higher doses. Based on the data from both studies in dog (results at the highest doses and the increase in trend with increased dosing) ocular discharge was considered to be compound related. In the 90-day rat study ocular findings were found in females at all dose levels on day 1. Experts agreed that for the 1-year dog study the NOAEL in males was 15 mg/kg bw/day (based on reduced body weight gain). In females, 15 mg/kg bw/day was considered to be a LOAEL.

Overall, the relevant short term toxicity NOAELs are 2 mg/kg bw/day (rat) and <15 mg/kg bw/day (dog).

2.4. Genotoxicity

Proquinazid manufactured by the old process (batch KQ926-45) was tested for genotoxicity, showing negative results with the exception of an *in vitro* mammalian cell gene mutation study whose findings could not be interpreted. A bacterial reverse mutation test, an *in vitro* mouse lymphoma assay and an *in vivo* mouse micronucleus assay were conducted with proquinazid manufactured by the current process (batch KQ926-75) and gave negative results. Overall, proquinazid did not show any genotoxic potential.

2.5. Long-term toxicity and carcinogenicity

Long term toxicity of proquinazid was tested in both rats and mice. Both species showed follicular hyperplasia and hypertrophy of the thyroid, with associated thyroid hormone changes (only investigated in rats), and some hepatic lesions (including necrosis and hyperplasia). Brown teeth, discoloured mucous membranes and dark red eyes in rats were regarded as adverse since they are cosmetically undesirable in humans. Ovarian cysts were increased in incidence at the top dose in rats and there was equivocal evidence for increased chronic progressive nephropathy at the top dose in

mice. The relevant NOAEL for long term toxicity is 1.2 mg/kg bw/day (30 ppm) from the rat study. The increased incidences of thyroid and liver tumours in rats (equivocal evidence in mice) were considered due to a non-genotoxic mechanism. The thyroid tumours were considered to occur via the induction of the liver UDP-glucuronyltransferase, with rodents being more sensitive to altered thyroid hormone homeostasis than humans; based on this, and the low potency of proquinazid for causing the effect in rats, it was concluded that the thyroid follicular adenomas were not relevant for humans. Increased incidences of hepatocellular adenomas and intestinal- type "cholangiocarcinomas" in female rats occurred at doses (>600 ppm) where there was systemic toxicity (considerably reduced body weight gain and marked liver toxicity). Significant hepatotoxicity was regarded as necessary for the development of cholangiofibrosis and the related intestinal-type "cholangiocarcinomas". Both tumours were considered of limited relevance for human risk assessment (note: there is some uncertainty as to whether these "cholangiocarcinomas" are tumours) . However, they were regarded as relevant for hazard-based classification. Proquinazid was proposed for classification as **R40 "Limited evidence of a carcinogenic effect".**

2.6. Reproductive and developmental toxicity

In a multigeneration study with proquinazid manufactured by the current process, no substance-related effects on reproductive parameters or organs in adult rats occurred (a marginal reduction in total litter weight occurred in F1 pups during lactation, likely secondary to maternal toxicity). During the meeting it was noted that only the multigeneration study with the current batch was evaluated in the DAR, even though the study conducted with material from the old production process showed higher toxicity than the current one. The RMS explained that the "old" study was not considered necessary for the risk assessment of the material from the current production process. As the "old" material was less purified than the new one, it was considered as not representative.

The parental and reproductive NOAELs are 2 mg/kg bw/day and 35 mg/kg bw/day, respectively; the offspring NOAEL is 11 mg/kg bw/day based on reduced litter weight.

Proquinazid is not teratogenic in developmental studies in rats and rabbits. In both species, evidence of decreased foetal weight was seen in the presence of maternal toxicity. Although proquinazid from the current production process was not tested in a developmental toxicity study, the evidence indicated that it would not have specific effects on development. The maternal and developmental NOAELs are 30 mg/kg bw/day (rat) and 2.5 mg/kg bw/day (rabbit), respectively.

2.7. Neurotoxicity

Based on studies with the old production process, it was considered that proquinazid is not neurotoxic.

2.8. Further studies

Metabolites

IN-MM671 is not present in the rat metabolism; it is of low acute oral toxicity to rats (LD_{50} >2000 mg/kg bw) and is not genotoxic in an *in vitro* bacterial gene mutation assay and an *in vivo* mouse bone marrow micronucleus assay.

Mechanistic studies

Mechanistic investigations during the chronic rat study showed that cytochrome P450 content and peroxisome proliferation were increased in rodent liver after 1 week, with lower increases after exposure for 6 or 12 months. No cellular proliferation was detected in the liver of rats when investigated after 1 week.

A study of the mechanism of thyroid effects in rats provided evidence for induction of the liver UDP-glucuronyltransferase and consequent changes in thyroid hormone levels.

2.9. Medical data

Proquinazid was produced on a pilot scale between 1996 and 1998 but has not been manufactured on an industrial scale for commercial use. No illnesses have been attributed to exposure through handling, testing, or manufacturing of proquinazid. No accidental poisonings with proquinazid have been reported.

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

ADI

An ADI of 0.01 mg/kg bw/day is proposed for proquinazid based on applying a 100-fold safety factor to the NOAEL of 1.2 mg/kg bw/day in the 2-year rat study.

ARfD

In the DAR an ARfD of 0.2 mg/kg bw was proposed for proquinazid based on applying a 100-fold safety factor to a dose level of 500 ppm (= 19 mg/kg bw/day for the first week of exposure) at which an increased incidence of ocular discharge was seen in one dog at the time of first exposure in a 90-day dietary study.

During PRAPeR 69 this proposal was discussed. One Member State proposed an ARfD of 0.3 mg/kg bw based on the developmental toxicity study in rats. In the rat study at a dose of 60 mg/kg bw/day a loss in bodyweight and reduced feed consumption occurred (NOAEL = 30 mg/kg bw day). However, as the findings in the 90-day dog study were considered to be adverse (although the mechanism is unclear) the majority of experts agreed to be conservative and to use the dog study for setting the ARfD. As the effect observed in this study at 19 mg/kg bw/day was minimal and present in only 1 animal, it was agreed to use the standard 100-fold safety factor. The agreed ARfD is 0.2 mg/kg bw.

AOEL

A systemic AOEL of 0.02 mg/kg bw/day is proposed for proquinazid based on applying a 100-fold safety factor to the NOAEL of 2 mg /kg bw/day determined in a 90-day dietary rat study.

2.11. Dermal absorption

The dermal absorption of the formulated product Proquinazid 200 g/L EC was investigated under *in vitro* and *in vivo* studies in the rat and an *in vitro* study with human skin. In the DAR, the RMS proposed a dermal absorption value of 2% proquinazid (concentrate) for operator exposure estimations for mixing/loading and 12% for spraying the formulated diluted product.

During PRAPeR 69 the proposal was agreed on by the experts.

2.12. Exposure to operators, workers and bystanders

Applications of Proquinazid 200 g/L EC will be achieved via field crop (boom) sprayers (cereals) and variable geometry boom sprayers (grapes), broadcast air assisted sprayers (grapes) and knapsack sprayers (grapes).

Operator

Model	Method	% of the AOEL No PPE	% of the AOEL With PPE
German model	Cereals - Tractor-mounted / trailed boom sprayer (hydraulic nozzles)	21	-
German model	Grapes - Tractor mounted/trailed broadcast air-assisted sprayer	62	-
German model	Grapes – Hand-held sprayer: hydraulic nozzles.	50	
UK POEM	Cereals - Tractor-mounted / trailed boom sprayer (hydraulic nozzles)	254	39*
UK POEM	Grapes - Tractor mounted/trailed broadcast air-assisted sprayer (low volume, 100 L/ha)	264	162*
UK POEM	Grapes - Tractor mounted/trailed broadcast air-assisted sprayer (high volume, 500 L/ha)	330	222*
UK POEM	Grapes – Hand-held sprayer, (15 lt Tank), hydraulic nozzles	377	172*
UK POEM	Grapes – Hand-held sprayer, (15 lt Tank), hydraulic nozzles	377	69^

*gloves when mixing and loading and during application
^gloves when mixing and loading and during application, impermeable coveralls during application

During PRAPeR 69 the proposal of the RMS to use EUROPOEM data to refine the exposure assessment via broadcast air assisted sprayers using UK POEM was considered acceptable.

Estimates of exposure during application to grapes via broadcast air-assisted sprayers were derived from refined UK POEM estimates of exposure using data from the EUROPOEM database.

Model	Method	% of the AOEL No PPE	% of the AOEL With PPE
EUROPOEM (75th percentile exposure data for grapevine spraying) UK POEM (mixing and loading)	Grapes - Tractor mounted/trailed broadcast air-assisted sprayer	53	-
EUROPOEM (maximum exposure data for grapevine spraying) UK POEM (mixing and loading)	Grapes - Tractor mounted/trailed broadcast air-assisted sprayer	154	20°

°Gloves and coveralls when handling the concentrate and during application

The estimates indicate the systemic exposure to proquinazid for operators to be within the systemic AOEL of 0.02 mg/kg bw/day even without PPE (for the German model only).

Bystander

Estimates of exposure to proquinazid for bystanders based on published simulated bystander exposure studies related to the use of field crop sprayers (Lloyd and Bell, see The United Kingdom, 2006, Vol.3 B.6.14.2) and broadcast air-assisted sprayers (Lloyd, Bell, Samuels, Cross and Berrie, see The United Kingdom, 2006, Vol.3 B.6.14.2) indicated exposure below the AOEL (12.3% and 0.75% for grapes and cereals respectively).

Worker

Estimates of exposure to proquinazid for workers were based on the German re-entry model proposed by Hoernicke *et al* (see The United Kingdom, 2006, Vol.3 B.6.14.2). The model was refined to address the potential accumulation of DFR for vines following successive treatments of 'Proquinazid 200 g/L EC' using data from a dislodgeable foliar residue study on outdoor vines grown in USA. Estimates indicate systemic exposure equivalent to 4% and 0.3% of the systemic AOEL, respectively.

3. Residues

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

Metabolism of [phenyl-^{14}C (U)] proquinazid was investigated in grapes and in wheat under outdoor field conditions. The study design was relevant to the proposed representative GAPs with application at moderately exaggerated rates.

In **wheat** (treated at 3N rate), parent proquinazid was the most significant component in grain (0.12 mg/kg) and the metabolite IN-MW977[15] (isomers of mono-hydroxy proquinazid) was the most significant component in forage, hay and straw (0.27 mg/kg, 0.40 mg/kg and 1.5 mg/kg respectively). Small amounts of other compounds were also present, mainly formed by further oxidation and conjugation steps.

It is noted that IN-MW977 consists of two optical isomers (enantiomers). It should also be noted that the methods of analysis used in all the residue studies were not stereoselective. Thus the regulatory dossier provides no information on the behaviour of each individual IN-MW977 enantiomer in plants. Therefore, all residues reported as IN-MW977 in this section of the conclusion are for the sum of the two enantiomers. It is not known if either isomer is metabolised or degraded more quickly than the other in the matrices studied.

Proquinazid residues ranged from 5% TRR (0.08 mg/kg) in hay to 35% TRR (0.12 mg/kg) in grain. IN-MW977 isomers residues ranged from 15% TRR (0.05 mg/kg) in grain to 35% TRR (0.27 mg/kg) in the forage. The glucose conjugate of IN-MW977[16] was found at 2-3% TRR (0.10 mg/kg and 0.01 mg/kg) in straw and grain respectively, and at 10% TRR (0.08 mg/kg) in forage. Other minor metabolites IN-MU210, a carboxylic acid metabolite, IN-MY341[17] (dihydroxylated) and IN-MM986 (O-dealkylated proquinazid) fraction P2 (tentatively identified as IN-MY340[18]) were also identified. 13% TRR in wheat straw were assumed to be associated with lignin.

In **grapes** (treated at 2N rate), proquinazid accounted for the majority of the extractable radioactivity (35-39% TRR, 0.08 – 0.09 mg/kg, day 0 to 29). The metabolite IN-MM671 was found in the grapes at 8.2% TRR (0.02 mg/kg) at day 29. A minor metabolite, IN-MM991 (2.3% TRR, 0.005 mg/kg), was

[15] IN-MW977: 2-{[(2*RS*)-2-hydroxypropyl]oxy}-6-iodo-3-propylquinazolin-4(3*H*)-one
[16] IN-MW977-glucose conjugates: (2*RS*)-1-[(6-iodo-4-oxo-3-propyl-3,4-dihydroquinazolin-2-yl)oxy]propan-2-yl β-D-glucopyranoside
[17] IN-MY341: 3-[(2*RS*)-2-hydroxypropyl]-2-{[(2*RS*)-2-hydroxypropyl]oxy}-6-iodoquinazolin-4(3*H*)-one
[18] IN-MY340: 2-{[(2*RS*)-2,3-dihydroxypropyl]oxy}-6-iodo-3-propylquinazolin-4(3*H*)-one

also identified. The amount of total radioactivity as well as the individual amounts of proquinazid and its metabolites found on the grapes remained relatively constant over the testing period.

The majority of the unextractable radioactivity (32% TRR) could be released upon strong alkaline treatment. The applicant postulated this radioactivity (23% TRR) was lignin incorporated, according to similar findings in a metabolism study in apples.

However, the apple study had not been evaluated in the DAR due to its submission late in the process and was therefore not available for peer review. As requested by the meeting of experts PRAPeR 70 the metabolism study in apple was evaluated in the addendum 3 of July 2009. The procedures applied in this study to isolate Björkman lignin and dioxane acidolysis lignin were described. Based on comparative characterisation of the alkaline soluble fractions of unextractable radioactivity in the apple study and in the grape study, the applicant assumed the presence of about 23% of the TRR in grapes as lignin. The RMS and EFSA believe this assumption is reasonable. It should be noted that the metabolism study in apples in addendum 3 is not peer reviewed and further findings of this study are not taken into account in this document.

Based on the available metabolism data, the main metabolic reactions in the metabolism of proquinazid in wheat plants were hydroxylation, carboxylic acid formation and conjugation, N- and O-dealkylation. The significant residues in the various wheat fractions were proquinazid and the metabolite IN-MW977 that was a major metabolite. In/on grape berries, proquinazid was only slowly metabolised by dehalogenation and O-dealkylation reactions to form minor amounts of IN-MM671 and IN-MM991. Thus, the overall picture of metabolism was found to be slightly different in wheat and grapes.

The proposed residue definition for consumer risk assessment for cereals and grapes should include proquinazid and metabolite IN-MW977. Though IN-MW977 was not detected in grapes, EFSA and the RMS agreed that a common residue definition should be proposed for both crops, grapes and cereals.

Since the toxicological reference values of proquinazid can be applied to metabolite IN-MW977, residues of proquinazid and metabolite IN-MW977 should be expressed as proquinazid.

The proposed residue definition for plant products for enforcement monitoring for cereals and grapes is proquinazid alone. A conversion factor of 2 is necessary to conduct the risk assessment for cereals based on broadly equivalent residues of proquinazid and the metabolite IN-MW977 as seen in the residue trials. For grapes the conversion factor should be 1 as metabolite IN-MW977 was virtually not present in grapes in the metabolism study.

3.1.2. Succeeding and rotational crops

To address potential residues in succeeding crops a confined rotational crop study was conducted using phenyl-^{14}C (U) proquinazid at a rate corresponding to approximately 3 fold the application rate notified for the representative use in wheat.

The soil was aged for 45 days and 210 days after the 2nd application and rotational crops (wheat grain, soybean seed, oilseed rape seeds and beet roots) were planted.

Significant total residues were detected in feed items, e.g. soybean (0.137 mg/kg in straw) and wheat (0.056 mg/kg in forage and 0.210 mg/kg in straw), while residues were low in crop parts for human consumption (all <0.01 mg/kg).

Analysis of samples with residues >0.01 mg/kg indicated the presence of multiple components. The levels of components present in the crops were not determined, thus only ‘qualitative’ information was

available. Levels were tentatively assigned to metabolites IN-MM671, IN-MT711[19], IN-MT712[20], IN-NC147[21], and IN-NC146[22] and anthranilic acid[23].

The meeting PRAPeR 70 considered that the parent is persistent in soil and that in particular metabolite IN-MM671 is very persistent in soil (DT_{90} >1 yr), and that metabolite IN-MM671 is present in the soil up to 65% of the applied radioactivity after 120 days. The study does not include results for the plant back interval of 365 days. Given the persistency of proquinazid and IN-MM671 in soil the RMS was requested to assess the maximum concentration of parent and metabolite in the soil considering potential accumulation.

An addendum (July 2009) was provided but not peer reviewed.

Therefore a final peer reviewed conclusion on whether significant amounts of metabolites may be expected in succeeding crops (mainly feed items) could not be drawn.

3.2. Nature and magnitude of residues in livestock

The metabolism and distribution of proquinazid was investigated in goats dosed for three consecutive days at a rate of 91.5 mg/kg diet (ca 175 N). The majority of the dose administered was found to be present in the excreta at 63% (urine, faeces, urea and cage wash). As the metabolism study was only conducted over three days it is not possible to conclude on when a plateau was reached.

Extractability of radioactivity was high for all commodities. The main metabolite found was IN-MU210 (also a major urinary metabolite), with other minor components found (proquinazid, IN-MY788[24]/IN-MY341, IN-MU715[25], IN-NA251[26] and IN-NA252[27]). The applicant has proposed a metabolic pathway based on proquinazid being extensively metabolised in goats primarily by oxidation of the propyl and propoxyl side-chains.

The goat metabolism study was conducted at 175 N rate with the major component being identified as the metabolite IN-MU210 (also a rat metabolite). This metabolite was found to be present in kidney at 0.84 mg/kg. Other matrices from the goat metabolism study also contained this metabolite but at lower levels (milk (0.17 mg/kg), liver (0.30 mg/kg), fat (0.03 mg/kg) and muscle (0.02 mg/kg)).

It was however noted by the experts in PRAPeR 70 that in cereals one major metabolite IN-MW977 was found (1/3 parent, 2/3 metabolite in cereal straw). This metabolite was also found in the ruminant fat (24% TRR), but the ruminant study was only carried out with the parent. Higher levels of the metabolite IN-MW977 in ruminant matrices could be expected when cereal commodities are used in animal feeding.

The metabolism and distribution of proquinazid was investigated in hens dosed for five consecutive days at a rate of 1.95 mg proquinazid/hen/day (ca 330N). The majority of the dose administered was found to be present in the excreta at 88%. It was not possible to deduce when a plateau may have been reached in eggs as residues increased over the period of the study (five days). The principal component in eggs was IN-NA250[28] (0.04 mg/kg). Other minor components were detected in eggs,

[19] IN-MT711: 3-(3-hydroxypropyl)quinazoline-2,4(1*H*,3*H*)-dione
[20] IN-MT712: 3-(2-hydroxypropyl)quinazoline-2,4(1*H*,3*H*)-dione
[21] IN-NC147: 3-(2,4-dioxo-1,4-dihydroquinazolin-3(2*H*)-yl)propanoic acid
[22] IN-NC146: 2-amino-*N*-propylbenzamide
[23] anthranilic acid: 2-aminobenzoic acid
[24] IN-MY788: 3-[2-{[(2*RS*)-2-hydroxypropyl]oxy}-6-iodo-4-oxoquinazolin-3(4*H*)-yl]propanoic acid
[25] IN-MU715: 3-(6-iodo-2,4-dioxo-1,4-dihydroquinazolin-3(2*H*)-yl)propanoic acid
[26] IN-NA251: 3-[(2*RS*)-2,3-dihydroxypropyl]-6-iodoquinazoline-2,4(1*H*,3*H*)-dione
[27] IN-NA252: (2*RS*)-2-hydroxy-3-(6-iodo-2,4-dioxo-1,4-dihydroquinazolin-3(2*H*)-yl)propanoic acid
[28] IN-NA250: 6-iodo-3-(2-oxopropyl)quinazoline-2,4(1*H*,3*H*)-dione

proquinazid (0.02 mg/kg), IN-MW398[29], IN-MW397[30], IN-MY340, IN-NA251 and IN-MM986 (all representing <0.02 mg/kg). In tissue (liver and muscle), the major component found was IN-MW398 at levels of 0.006 mg/kg to 0.039 mg/kg. The applicant has proposed a metabolic pathway based on proquinazid undergoing oxidation to yield a combination of metabolites containing mono- and di-hydroxy and carboxylic acid functional groups. The applicant states that the metabolism in the hens was more extensive than seen in the rat and goat. In comparison to the rat and goat studies higher concentrations of metabolites IN-NA250, IN-NA251, IN-MW397 and IN-MW398 resulting from side-chain cleavage reactions (O- and N-dealkylation) were observed in hen tissues and/or excreta.

On the basis of the available data no residues >0.01 mg/kg are expected in hen tissues. However, doubts exist concerning the plateau which was not reached in the eggs. The experts agreed that if a metabolism study is necessary for future uses, the study should be carefully reassessed.

It was agreed that the following residue definition in animal matrices should be proposed for risk assessment: Sum of proquinazid and metabolites IN-MU210 and IN-MW977 expressed as proquinazid.

For monitoring, it was agreed that the following residue definition in animal for monitoring matrices should be proposed: Sum of proquinazid and metabolite IN-MU210, expressed as proquinazid.

Animal feeding studies have not been submitted. Animal metabolism studies have been conducted at exaggerated rates. Acknowledging uncertainties when extrapolating from studies with exaggerated doses, it was yet agreed that residues are not expected to exceed 0.01 mg/kg in animal products, considering the intake from the notified representative uses.

On the basis of the proposed residue definition for monitoring risk managers may consider to set MRLs for a fat-soluble residue in food of animal origin on the LOQ of the analytical method for monitoring (see data requirement in section 1).

3.3. Consumer risk assessment

Chronic intake

The TMDIs calculated using the consumption data available on the WHO standard European diet show that intakes are well below the ADI of 0.01 mg/kg bw/day. The total TMDI is <2% of the ADI.

Using UK consumption data, chronic exposure estimates for long term dietary exposure intakes are well below the ADI of 0.01 mg/kg bw/day. The total NEDIs vary according to different consumer groups, the values range from 3% (elderly residential) to 22% (toddlers) of the ADI.

Acute intake

Using UK consumption data acute exposure estimates for short term dietary intakes are well below the ARfD of 0.2 mg/kg bw/day. The highest NESTI for cereals was wheat/4-6 year olds, toddlers and infants at 0.3% of the ARfD. In grapes, NESTIs were up to 27.8% of the ARfD

3.4. Proposed MRLs

Grapes	0.5 mg/kg
Barley	0.05 mg/kg

[29] IN-MW398: 6-iodoquinazoline-2,4(1*H*,3*H*)-dione
[30] IN-MW397: 3-[(2*RS*)-2-hydroxypropyl]-6-iodoquinazoline-2,4(1*H*,3*H*)-dione

Rye	0.05 mg/kg
Wheat	0.05 mg/kg
Oats	0.05 mg/kg
Triticale	0.05 mg/kg

The MRLs proposed are for proquinazid in cereals and proquinazid only in grapes. A conversion factor of 2 is needed to conduct the risk assessment for cereals based on broadly equivalent residues of proquinazid and the metabolite IN-MW977 as seen in the residue trials; the factor for grapes is 1.

4. Environmental fate and behaviour

Fate and behaviour of proquinazid into the environment was discussed in the meeting of experts PRAPeR 67 based on the DAR and the addendum 2 (March 2009).

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

The route of degradation of proquinazid (^{14}C labelled in the phenyl ring) in soil under aerobic conditions at 20 ºC was investigated in two studies with a total of four soils (pH 5.5 – 7.3, OC 0.64 – 1.9 %, clay 4 – 21.6 %). The only major metabolite observed was IN-MM671 (max 65 % AR after 120 d) that resulted from the loss of the iodine atom. This was followed by the dealkylation of the oxygen atom to form the quinazolinedione IN-MM991 (max. 7 % AR after 210 d). This metabolite was observed in one of the soils at levels above 5 % AR in two consecutive sampling dates and therefore has been assessed for potential ground water contamination. The quinazolinedione product of dealkylation of the parent proquinazid IN-MM986 was also observed as a minor metabolite in soil (max. 8 % AR after 183 d). Mineralization was negligible in one of the soils and reached maximum levels of 2 – 28 % AR after 365 d in the three other soils. Unextractable residues at the end of the study (1 yr) reached levels up to 15 – 32 % AR. The majority of the unextractable radioactivity was associated with the humic or humin acid fractions and to lesser extend with the fulvic acid fraction.

A water/sediment study under dark anaerobic conditions was provided as surrogate of the study of degradation in soil under anaerobic conditions. In this study, the degradation of proquinazid ^{14}C labelled at the phenyl ring was investigated in one water sediment system (pH_{water} = 8.8 ; $pH_{sediment}$ = 6.5, OM 1.6 %, clay 3 %). The same metabolites identified under aerobic conditions were found in this anaerobic study. Unextractable residues in the sediment amounted to 22.6 % AR at the end of the study (1 yr). No significant mineralization was observed under these conditions (1.3 % AR as CO_2 after 365 d).

The photo degradation of proquinazid ^{14}C labelled at the phenyl ring was investigated in one microbially active soil (pH 6, OC 1.9 %, clay 8.8 %) at 20 ºC. Degradation of proquinazid was significantly enhanced by the irradiation of a light source simulating midday June sunlight in Phoenix, Arizona (USA, Latitude 33º26' N). Metabolite IN-MM671 was the main metabolite (max. 14.45 % AR after 168 h of continuous irradiation).

Dissipation of proquinazid was investigated in four field dissipation studies in a total of eight European sites (2 in UK, 2 in Northern France, 2 in Southern France, 1 in Italy, 1 in Germany). Proquinazid ^{14}C labelled at the phenyl ring was applied in one of the studies (Alconbury, UK). In the other sites, it was applied as emulsifiable concentrate formulations containing non labelled proquinazid and DPX-KZ165 (a substance under development at the time of the study that has not been commercialized).

Higher concentrations of metabolites were found in the field studies with respect to the laboratory ones. The metabolites **IN-MM671, IN-MM991** and **IN-MM986** appeared at levels above 10 % AR at various sampling points in the radiolabelled study. In the non radiolabelled trials only IN-MM671 and IN-MM986 were found consistently above 10 % of the applied amount.

Three soil residue studies are available. Residues in soil are investigated in 16 EU sites (2 in Northern France, 6 in Southern France, 4 in Germany, 2 in Italy, 1 in Belgium and 1 in UK).

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

The rate of degradation of proquinazid and its major metabolite IN-MM671 under dark aerobic conditions at 20 ºC was calculated with data from the same studies that investigated the route of degradation in soil. The applicant used multicompartmental modelling assuming first order for both the parent and the major metabolite (SFO/SFO). Proquinazid exhibits moderate to high persistence ($DT_{50\ lab\ 20\ ºC}$ = 39.5 – 345 d) under these conditions. Metabolite IN-MM671 is highly persistent in soil under aerobic conditions in these studies ($DT_{50\ lab\ 20\ ºC}$ = 170 – 223 d). For this metabolite no reliable half-life was obtained from one of the soils (Speyer soil).

In a separate study, the rate of degradation of the three soil metabolites was investigated in three soils (pH 5.7 – 8.1, OC 0.59 – 1.9 %, clay 7.2 – 22.8 %) under dark aerobic conditions at 20 and 10 ºC. In this study the major metabolite IN-MM671 is medium persistent in soil at 20 ºC ($DT_{50\ lab\ 20\ ºC}$ = 71 – 94 d), IN-MM986 is moderately persistent in soil ($DT_{50\ lab\ 20\ ºC}$ = 16 - 36 d) and metabolite IN-MM991 is moderately persistent in soil ($DT_{50\ lab\ 20\ ºC}$ = 21 – 30 d).

In the anaerobic water / sediment study proquinazid was medium persistent (DT_{50} = 61 d).

Photolysis may contribute to the environmental degradation of proquinazid (DT_{50} = 19 d of continuous irradiation, corrected for degradation in the dark control).

All field dissipation trials were performed on bare soil, therefore contribution of photolysis to certain extend may not be excluded. In these trials proquinazid was low to medium persistent in soil ($DissT_{50}$ = 5.5 – 70 d), IN-MM671 was moderate to very highly persistent in soil ($DissT_{50}$ = 29 – 394 d), IN-MM986 was moderately to medium persistent ($DissT_{50}$ = 34 – 68.5 d) and IN-MM991 moderately persistent ($DissT_{50}$ = 54 d, Pompignan site). The meeting of experts identified another field study where this metabolite appeared at levels of 13.5 % (Alconbury site, Eversham soil) and requested the RMS to calculate the half-life of this metabolite in that field site. This updated half-life has been provided in the List of end points ($DissT_{50}$ = 104 d, Alconbury site).

The PEC soil values provided in the dossier by the applicant were based on kinetic parameters derived from the laboratory studies. The RMS recalculated PEC soil based on kinetic data derived from the field studies. The RMS calculated the PEC soil value using the proquinazid worst case half-life value and the maximum metabolite amount observed in field studies.

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

Batch adsorption / desorption studies in soil are available for proquinazid and its metabolites IN-MM671, IN-MM991 and IN-MM986.

Adsorption / desorption characteristics of proquinazid (^{14}C radiolabelled at the phenyl ring) was investigated in four soils (pH 5.3 – 7.3, OC 0.6 – 2.1 %, clay 2.8 – 24 %). Adsorption / desorption characteristics of non labelled metabolites IN-MM671, IN-MM991 and IN-MM986 were also investigated in four different soils (pH 5.2 – 8.0, OC 0.6 – 1.9 %, clay 5.2 – 8.0 %). According to the results of these studies, proquinazid may be considered as immobile in soil (K_{oc} = 9091 – 16769

mL/g), IN-MM671 as slightly mobile (K_{oc} = 2333 - 4167 mL/g), IN-MM991 as medium to highly mobile (K_{oc} = 137 - 342 mL/g) and IN-MM986 as slightly to low mobile (K_{oc} = 1368 - 2500 mL/g) in soil.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Hydrolytic stability was investigated for proquinazid and the metabolites IN-MM671, IN-MM991, IN-MM986 and the aqueous photolysis metabolite IN-MT884[31] in sterile buffered aqueous solutions (pH 4, 7 and 9) at 20 °C. Proquinazid and all the metabolites investigated were stable to hydrolysis under the tested conditions. It is not expected that hydrolysis will contribute to the environmental degradation of proquinazid and its metabolites.

Aqueous photolysis of proquinazid was investigated in one study with artificial light simulating mid-day light in Concord, Ohio (USA, 40° N) in a buffered solution (pH 7) at 20 °C. Proquinazid is rapidly photolysed in water under the study conditions (DT_{50} < 1 h). Major photolysis metabolites identified were IN-MM671 (max. 17.2 % AR after 4 h), IN-MM991 (max. 14.2 % AR after 1 h), IN-MM986 (max. 14.5 % AR after 2 h) and IN-MT884 (max. 30.5 % AR after 1 d). Theoretical photolysis half-lives of proquinazid and its metabolites in the top layer (0.001cm) of an aqueous system integrated over a full summer day at 40° latitude were calculated based on the results of this study ($DT_{50\ (proquinazid)}$ = 1 h; $DT_{50\ (IN\text{-}MM671)}$ = 16.1 d; $DT_{50\ (IN\text{-}MM991)}$ = 12.7 d; $DT_{50\ (IN\text{-}MM986)}$ = 32.8 d; $DT_{50\ (IN\text{-}MT884)}$ = 132 d). Reliability of photolysis half-lives of metabolites IN-MM991 and IN-MT884 is questioned by the RMS due to bad fitting practice (IN-MM991) and the short number of data available after the maximum is reached (IN-MT884).

The ready biodegradation of proquinazid was investigated according OECD guidelines (301/B)(OECD, 1992). According to this study proquinazid is not considered to be readily biodegradable.

The degradation and metabolism of ^{14}C labelled proquinazid in aquatic environment was investigated in a study with two separate dark water / sediment systems (pH_{water} = 7.2 – 7.5; pH_{sed} = 7.2 – 7.3, OM_{sed} = 0.9 – 2.9 %, $clay_{sed}$ = 9 - 17 %) at 20 °C. In both systems, proquinazid partitioned rapidly into the sediment ($DissT_{50}$ < 1 d). However, it is moderately to highly persistent in the total system (DT_{50} = 36.5 – 136 d). The only metabolite identified was IN-MM671 (max 68 % AR in the sediment after 100 d, end of the study) that is very highly persistent in both systems (DT_{50} > 500 d). However this metabolite is strongly absorbed to the sediment and only amounts up to 6 % AR (after 30 d) are found in the water phase. Mineralization was practically negligible (CO_2 0.2 - 1.4 % AR) and unextracted residues in the sediment ranged between values of 5 to 15 % AR during all the experiments. The majority of the unextracted residue was associated to the fulvic acid fraction of the sediment.

PEC_{SW} were calculated by the applicant following the FOCUS SW scheme. Step 1 and 2 were calculated for the metabolites IN-MM986, IN-MM991 and IN-MT884. FOCUS SW Step 3 was calculated for proquinazid and the metabolite IN-MM671. The RMS recalculated Step 3 with more adequate application windows. For each use (winter cereals, spring cereals, early and late applications on grapes) the worst case PEC (global maximum PEC_{SW} and PEC_{SED}) in the respective FOCUS SW scenario (D1, D2, D3, D4, D5, D6, R1, R2, R3 or R4) is reported for its use in the risk assessment. Since spray drift is deemed to be the main route of entry of proquinazid in surface water FOCUS Step 3 calculations were performed using both multiple and single application spray drift inputs. For all cereals and grapes, the maximum global PEC_{SW} results from the single application scenario. In contrast the maximum global PEC_{SED} always results from the multiple application scenarios. The

[31] IN-MT884: 4-(2-carboxyethyl)-6-oxo-2-propoxy-1-propyl-1,6-dihydropyrimidine-5-carboxylic acid

applicant also provided FOCUS Step 4 calculations by introducing buffer zones of 3 m for cereals and 14 m for grapes. Whereas FOCUS Step 4 methodologies to incorporate the assessment of potential mitigation measures were still not agreed at the time the dossier was prepared, mitigation of the spray drift by buffer zones was considered in this assessment. Consideration of buffer zone mitigation on spray drift was already standardised at the time the FOCUS scheme was developed. Therefore, its implementation on the FOCUS SW modelling is considered to be straightforward and acceptable. Also in this case, the RMS recalculated the FOCUS Step 4 for single and multiple applications with more adequate application dates. Default FOCUS Step 3 for pond scenarios in cereals is already 3.5 m and no Step 4 calculation was done for these scenarios. For ditch and stream scenarios, a 3 m buffer zone was calculated for Step 4 in cereals. A Step 4 modelling with a 14 m buffer zone was calculated for vine scenarios. In the case of three out of the six late vine scenarios (single application), risk assessment failed with the 14 m buffer zone and therefore the 16 m buffer zone was also calculated. In the Step 4 cereals and vines calculation, the maximum global PEC_{SW} results from the single application scenario. In contrast, the maximum global PEC_{SED} always results from the multiple application scenarios.

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

Potential groundwater contamination by proquinazid and its main soil metabolites was addressed by calculation of the 20 years 80th percentile leachate concentration at 1m depth on the FOCUS GW relevant scenarios for each of the representative uses proposed (winter cereals: 9 scenarios; spring cereals: 6 scenarios; grapes: 7 scenarios) with FOCUS GW PELMO 3.3.2. Two alternative degradation pathways were considered (with and without metabolite IN-MM986). The RMS repeated the calculation for winter cereals with more adequate application dates. The concentration of proquinazid and the metabolites IN-MM671, IN-MM991 and IN-MM986 were < 0.001 µg / L for all the uses and scenarios simulated.

4.3. Fate and behaviour in air

Proquinazid has a vapour pressure of 9 x 10^{-5} Pa (25 ^{o}C) and a calculated Henry's Law constant of 3 x 10^{-2} Pa·m^3 / mol. Volatilisation from dry soils appears to be insignificant from the available studies. However, volatilisation from plant surface was up to 14 % AR. Nevertheless, no atmospheric long range transport is expected for proquinazid because the calculated half-life for photochemical oxidative degradation in the atmosphere was calculated to be 4 h.

5. Ecotoxicology

Proquinazid was discussed in the PRAPeR experts' meeting for ecotoxicology (PRAPeR 68) in May 2009, on the basis of the DAR, and the addendum 2 (March 2009).

The risk assessment was conducted according to the following guidance documents: Risk Assessment for Birds and Mammals. SANCO/4145/2000, September 2002 (European Commission, 2002a): Aquatic Ecotoxicology. SANCO/3268/2001 rev.4 final, October 2002 (European Commission, 2002b); Terrestrial Ecotoxicology. SANCO/10329/2002 rev.2 final, October 2002 (European Commission, 2002c); Risk Assessment for non-target arthropods. ESCORT (SETAC, 2001).

5.1. Risk to terrestrial vertebrates

A risk assessment for birds and mammals using the cereal and vine scenarios was performed.

First tier calculations of TERs for birds resulted in values far above the trigger for acute and short-term exposure in the standard scenarios. For the long-term, TER values were 5.16 for insectivorous

birds following an application of maximum 50 g a.s./ha in cereals, and 6.38 for large herbivorous birds. These values meet the Annex VI trigger of 5 and the risk is therefore considered to be low. However, following an application of 75 g a.s/ha in vine the TER_{lt} was 3.44 indicating a potential risk. The potential long-term risk for insectivorous birds in vine was refined by considering the Yellowhammer (*Emberiza citronella*) and the Cirl bunting (*Emberiza cirlus*), and their respective diets, as focal species for Central European and Southern European vineyards, respectively. As a worst case scenario, 100% of the summer diet for both species was considered to consist of arthropods (50% small insects and 50% large insects). The applicant argued that, if a 50:50 split between small and large insects was assumed, the mean (17.05) of these two RUD values (29 for the small insect and 5.1 for the large insect) should be used. Thus, a mean of the 'Residue unit dose' for small and large insects was used. The resulting TER_{lt} was 5.85 and hence the risk was concluded to be low.

As for birds, the acute risk to mammals was considered to be low. Also the long-term risk to mammals in cereals following an application of proquinazid was considered to be low based on TER values of 9.04 and 217.8 for small herbivorous and insectivorous mammals, respectively. The long-term risk to herbivorous mammals in vine following application of 75 g a.s./ha was considered to be low since the TER value was 8.72.

The metabolite IN-MM671 was detected in grape plant metabolism studies and the metabolite IN-MW977 in cereals. The latter metabolite was also identified as a metabolite in studies on rat, goat and possibly hen. Since IN-MW977 has a very similar structure to the parent and the parent is extensively metabolised to IN-MW977 being a significant metabolite, the risk from this metabolite to mammals was considered to be covered by the risk assessment for proquinazid. IN-MM671 was the major degradation product of proquinazid detected in soil and aquatic systems. IN-MM671 has a low acute oral toxicity to the rat and showed no genotoxicity. The acute risk to mammals is low. If a similar acute toxicity of IN-MM671 and proquinazid is also assumed for birds, the acute risk to birds from exposure to this metabolite would be covered by the risk assessment for proquinazid.

Besides IN-MM671, the metabolites IN-MM986 and IN-MM991 were detected in soil and in water. One additional metabolite, IN-MT884 was detected in the aquatic photolysis study. IN-MM671 partitioned to sediment in the water/sediment study. The most likely exposure route for the metabolites would be through ingestion of contaminated earthworms or fish. The log P_{ow} for the parent proquinazid is 5.5. The log P_{ow} for IN-MM671 is 3.42. No log P_{ow} was available for the other metabolites but the log P (HPLC) values were below 3 for IN-MM986 and IN-MT884. The Log P values determined by other methods were available for IN-MT884 and the other metabolites, and showed consistently lower values than for the other metabolites. Therefore only the parent proquinazid and the metabolite IN-MM671 were considered for the assessment of secondary poisoning of earthworm- and fish-eating birds and mammals.

For proquinazid used in cereals the TER for earthworm- and fish-eating birds and mammals met the Annex VI trigger for cereals without any refinements. However, the TER_s values for earthworm and fish-eating birds did not meet the Annex VI trigger values for the use in vine. The applicant proposed a method for refinement by using 21-day TWA PEC_{sw} from FOCUS step 3 modelling for fish-eating birds, resulting in a TERs values above the trigger value and thus indicating a low risk. The applicant proposed a refinement of the potential high risk for the earthworm-eating birds, by considering the 4 applications with different doses at different growth stages and corresponding interception factors (1st application BBCH <61, 2nd and 3rd applications BBCH 61-71, 4th application BBCH >71; application rates 40/60/60/75 g a.s./ha; interception factors 50/50/50/70 %). These new PEC_{soil} values based on the use of different interception factors were not presented in the DAR or in the addenda and were neither peer reviewed by the fate experts or checked by EFSA. Furthermore, EFSA noted after the peer review process that the refinement application scheme (4 x applications of 50 g proquinazid /ha) will not cover the representative uses for vines in Germany, Italy and Greece. Therefore, with the available information the risk for the earthworm-eating birds from the use in vines (as up to 4 applications at 75 g a.s./ha) could not be considered as low. A data gap was identified after the peer review process for

the applicant to submit further information to address the risk to earthworm-eating birds for the vine use.

The risk to earthworm- and fish-eating birds and mammals from exposure to the metabolite IN-MM671 is covered by the assessment for proquinazid if the toxicity is assumed to be the same.

Significant accumulation of contaminated water in leaf axils is not considered likely in treated cereals or vines and therefore the main source of proquinazid uptake via drinking water will be from contaminated surface waters. Maximum FOCUS Step 3 surface water PECs are reported to be 0.316 µg a.s./l (cereal use) and 1.311 µg a.s./l (vine use). These contamination levels in drinking water are much lower than the ones in foliage and insects from cereal use - estimated for acute exposure (individual dose x RUD x [for foliage only] MAF) to be 8.9 mg a.s./kg (foliage) and 2.6 mg a.s./kg (insects) - with higher residues likely from the higher applied dose in vines. Given the much higher residues in foliage and insects than in surface water, the dietary route of exposure is considered to be the main source of exposure. The assessment of the risk from the dietary route of exposure will therefore cover that from the intake of contaminated drinking water.

5.2. Risk to aquatic organisms

Proquinazid was considered to be very toxic to aquatic organisms, with the lowest EC_{50} (0.11 mg a.s./L) obtained for *Mysidopsis bahia*. The EC_{50} for the standard aquatic invertebrate test species *Daphnia magna* was 0.287 mg a.s./ha. Acute toxicity values in the same order of magnitude were derived also for fish and algae. The formulation 'Proquinazid 200 g/L EC' was not more toxic than expected based on the content of proquinazid. Since proquinazid has a log P_{ow}>3 and a bio concentration factor of 821 for whole fish, it may also cause long-term effects in the aquatic environment. The proposed classification for proquinazid is therefore **R50/53 "Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment"**.

Acute TERs for all aquatic organisms tested were above the respective Annex VI trigger based on FOCUS Step 1 initial PEC_{sw} for the use in cereals, except for *M . bahia*. The assessment for *M. bahia* was refined by using FOCUS Step 2 initial PEC_{sw} for a single application. The resulting TER was 239, hence indicating a low acute risk for the use in cereals. For the use in vine the first tier risk assessment indicated a potential risk with a TER_a of 8.1 for *M. bahia* based on Step 1 FOCUS $PEC_{sw.}$ With a 5 m buffer zone to reduce the input from spray drift in FOCUS Step 4 calculations, a TER_a of 115.2 was derived. The long-term TER values were below the Annex VI trigger for aquatic invertebrates in 11 out of 15 FOCUS Step 3 scenarios for cereals (TERs 5.7 – 164) and in 5 of the 6 scenarios for vine (TERs 1.4-38). FOCUS Step 4 calculations showed that non-spray buffer zones of 3 and 16 m for cereals and vine respectively are necessary to protect the aquatic environment in the worst case scenarios.

Three metabolites (IN-MM671, IN-MM986, IN-MM991) were formed in amounts >10% of the applied dose in soil or water/sediment. Additionally the metabolite IN-MT884 was detected in the aqueous photolysis study. Acute toxicity studies with fish, daphnids and algae were available for the three former metabolites. For IN-MT884, only a study with *D. magna* was available. The TER values indicated a low acute risk for all metabolites using FOCUS Step 1 PEC_{sw} concentrations. Even if IN-MT884 would be 1000 times more toxic to algae than to *D. magna*, the Annex VI trigger of 10 would still not be exceeded. From the results of a chronic study with IN-MM671 on *D. magna* and the FOCUS Step 1 PEC_{sw}, a low long-term risk was concluded for both cereals and vine. No studies on chronic toxicity to fish were available, but since *D. magna* was the most sensitive organism for proquinazid and the structures are very similar, the chronic fish study was considered not necessary. The long-term risk to the other metabolites was considered to be covered by the assessment for proquinazid since the acute toxicity was lower than for the parent and the structures are very similar.

Proquinazid and the metabolite IN-MM671 were detected in the sediment phase of the water/sediment study in amounts exceeding 10% of the applied dose and exposure of sediment dwelling organisms

cannot be excluded. The result from a chronic toxicity study with *Chironomus riparius* exposed to proquinazid in the water phase was compared to PEC_{sw} from FOCUS Step 1 assuming that the total load was present in the water phase. The TER obtained for cereals was 18.1, hence indicating a low risk. However, TER obtained for the use in vine was 5.73, which is below the Annex VI trigger. Using the PEC_{sw} from FOCUS Step 2 resulted in a TER of 35.4, so also the risk in vine was concluded to be low. Since the NOEC for *Daphnia magna* was >0.1 mg a.s./L for IN-MM671 no studies with *C. riparius* are required for the metabolite and the risk to sediment dwellers is considered to be low.

The bio concentration factor for proquinazid was determined as 821 for whole fish and as 483 for the metabolite IN-MM671. Depuration was however rapid for both the parent and the metabolite.

In conclusion, risk mitigation corresponding to spray free buffer zones of 3 m for the use in cereals and 16 m for the use in vine is required to protect aquatic organisms in all relevant FOCUS scenarios.

5.3. Risk to bees

The oral and contact acute toxicity of proquinazid and the formulation Proquinazid 200 g/L EC is low and the hazard quotients are below 1 for all evaluated uses. The risk to bees is therefore concluded to be low.

5.4. Risk to other arthropod species

LR_{50} values derived in glass plate laboratory tests with the standard species *Aphidius rhopalosiphi* and *Thyphlodromus pyri* using formulated Proquinazid 200 g/L EC were used to calculate in-field and off-field hazard quotients for non-target arthropods. All HQ values, except from the in-field for *T. pyri*, were below the ESCORT II trigger of 2.

The in-field risk to *T. pyri* was refined based on results from field studies in vineyards conducted in Germany, France and Italy with 4 applications of 75 g a.s./ha at different growth stages. The data from these studies indicated that there were no effects >50% at any time during testing, and there were no significant reductions in mite numbers at the end of the study period. The predatory mites identified in the German and French studies were between 99.2 and 100% *T. pyri*, while the Italian study had a range of species present. In the Italian study a change in relative percentages of the different species was noted in the proquinazid treated plots, compared to pre-treatment and post-treatment ratios in the control plots. None of the two major species (*Kampimodromus aberrans* and *Amblyseius andersoni*) were however entirely eliminated.

Additionally, extended laboratory studies with *A. rhopalosiphi, Chrysoperla carnea* and *Orius laevigatus* using fresh and aged foliar spray residues were available. The results from these studies showed <20% effect on mortality and reproduction.

It can be concluded that the risk to non-target arthropods is considered to be low.

5.5. Risk to earthworms

The acute risk to earthworms from exposure to technical proquinazid, the soil metabolites IN-MM671, IN-MM986 and IN-MM991 and the formulated product is considered to be low based on TER values well above the Annex VI trigger. The peak plateau PEC_{soil} was used in the calculations. Reproduction studies were available with formulated proquinazid and the metabolite IN-MM671. Based on the results from these studies, TER_{lt} values of 410 and 2083 were obtained for the use in cereals and 155 and 442 for the use in vine, for proquinazid and the metabolite respectively. No chronic studies were available with the other soil metabolites. However, the structures are similar to IN-MM671, for which the long-term TER was far above the Annex VI trigger, and the PEC_s is lower and the degradation

faster. EFSA agrees with the RMS that no further studies are required and that the risk to earthworms can be concluded to be low.

5.6. Risk to other soil non-target macro-organisms

No statistically significant effects on straw decomposition were detected in a litter bag study conducted with formulated proquinazid in Germany. The levels of proquinazid and the metabolites were considered to cover the maximum soil concentrations expected from the proposed uses. Therefore the risk to other soil macro-organisms is considered to be low.

5.7. Risk to soil non-target micro-organisms

The formulation Proquinazid 200 g/L EC had no effects >25% after 28 days on soil respiration or nitrogen turnover following treatments corresponding to 1× and 10× the maximum single field application rate proposed for vine. Neither did the soil metabolites IN-MM671, IN-MM986 and IN-MM991 had any effects >25% at soil concentrations above the initial or peak plateau PEC_{soil}. The risk to soil micro-organisms is therefore considered to be low.

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

No visual phytotoxic effects >50% were observed following post-emergence application of Proquinazid 200 g/L EC at a rate corresponding to 75 g a.s./ha to *Lolium perenne, Avena fatua, Allium cepa, Brassica napus, Glycine max* and *Beta vulgaris*. Additionally, no phytotoxic effects were reported on crop species in efficacy tests following post-emergence application of doses of 20-200 g a.s./ha. With respect to pre-emergence effects, application at 100 g a.s./ha in May in winter wheat crops resulted in no adverse effects to subsequent crops (2 cereals and 4 dicot species) planted 7-15 months later. In addition, information was provided from a 1995 greenhouse study in which pre or post-emergence use of Proquinazid 200g/l EC at 400 g a.s./ha resulted in no phytotoxic effects to a range of monocot and dicot non-crop plant species. Based on this information the risk to non-target plants from exposure to proquinazid and its metabolites is considered to be low.

5.9. Risk to biological methods of sewage treatment

The EC_{50} for inhibition of respiration rates of activated sludge was determined as >100 mg a.s./L. Should proquinazid reach sewage treatment facilities via waste water channels, the risk is considered to be low due to the low toxicity in the test.

6. Residue definitions

6.1. Soil

Definition for risk assessment: Proquinazid, IN-MM671[32], IN-MM986[33], IN-MM991[34]

Definition for monitoring: Proquinazid, IN-MM671, IN-MM986, IN-MM991

[32] IN-MM671: 2-propoxy-3-propylquinazolin-4(3*H*)-one
[33] IN-MM986: 6-iodo-3-propylquinazoline-2,4(1*H*,3*H*)-dione
[34] IN-MM991: 3-propylquinazoline-2,4(1*H*,3*H*)-dione

6.2. Water

6.2.1. Ground water

Definition for exposure assessment: Proquinazid, IN-MM671, IN-MM986, IN-MM991

Definition for monitoring: Proquinazid, IN-MM671, IN-MM986, IN-MM991

6.2.2. Surface water

Definition for risk assessment

in surface water: Proquinazid, IN-MM671, IN-MM986, IN-MM991, IN-MT884[35] (aqueous photolysis metabolite)

in sediment: Proquinazid, IN-MM671, IN-MM986, IN-MM991, IN-MT884 (aqueous photolysis metabolite)

Definition for monitoring: Proquinazid, IN-MM671, IN-MM986, IN-MM991

6.3. Air

Definition for risk assessment: Proquinazid

Definition for monitoring: Proquinazid

6.4. Food of plant origin

Definition for risk assessment: cereals, fruit: proquinazid and metabolite IN-MW97736 expressed as proquinazid

Definition for monitoring: proquinazid

6.5. Food of animal origin

Definition for risk assessment: sum of proquinazid and metabolites IN-MU210 and IN-MW977 expressed as proquinazid

Definition for monitoring: sum of proquinazid and metabolites IN-MU210 expressed as proquinazid

[35] IN-MT884: 4-(2-carboxyethyl)-6-oxo-2-propoxy-1-propyl-1,6-dihydropyrimidine-5-carboxylic acid
[36] IN-MW977: 2-{[(2*RS*)-2-hydroxypropyl]oxy}-6-iodo-3-propylquinazolin-4(3*H*)-one

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

6.6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Proquinazid	moderate to high (DT50 lab 20 ºC = 39.5 – 345 d)	Low risk was observed for the earthworms.
IN-MM671	medium to high (DT50 lab 20 ºC = 71 – 223 d)	Low risk was observed for the earthworms.
IN-MM986	moderate (DT50 lab 20 ºC = 16 - 36 d)	Low risk was observed for the earthworms.
IN-MM991	moderate (DT50 lab 20 ºC = 21 – 30 d)	Low risk was observed for the earthworms.

6.6.2. 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
Proquinazid	immobile (Koc = 9091 – 16769 mL / g)	No	Yes	Yes	Proquinazid was considered to be very toxic to aquatic organisms
IN-MM671	slightly mobile (Koc = 2333 - 4167 mL / g)	No	No	Not assessed, not needed	IN-MM671 was considered to be very toxic to aquatic organisms
IN-MM986	slightly to low mobile (Koc = 1368 - 2500 mL / g)	No	No	Not assessed, not needed	IN-MM986 was considered to be very toxic to aquatic organisms
IN-MM991	medium to high mobile (Koc = 137 - 342 mL / g)	No	No	Not assessed, not needed	IN-MM991 was considered to be toxic to aquatic organisms

6.6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Proquinazid (water and sediment)	High risk was identified for the aquatic organisms.
IN-MM671(water and sediment)	Low risk was identified for the aquatic organisms.
IN-MM986 (water and sediment)	Low risk was identified for the aquatic organisms.
IN-MM991 (water and sediment)	Low risk was identified for the aquatic organisms.
IN-MT884 (water and sediment, photolysis metabolite)	Low risk was identified for the aquatic organisms.

6.6.4. Air

Compound (name and/or code)	Toxicology
Proquinazid	Not acutely toxic via inhalation

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

- A revised specification or a justification concerning the minimum purity and the maximum limits of the impurities 1, 2 and 3 from the table C.1.2 of the Addendum 2 to vol. 4, (relevant for all representative uses evaluated, data gap identified by PRAPeR 66 meeting (April 2009), date of submission unknown; refer to chapter 1)

- Further information to address the risk to earthworm-eating birds (relevant for the intended use in vine, data gap identified by EFSA after the peer review, date of submission unknown; refer to section 5.1)

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

The conclusion was reached on the basis of the evaluation of the representative uses as fungicide as proposed by the applicant against powdery mildew in wheat, barley, oats, triticale, rye and grapes. For full details of the GAP please refer to the end points in Appendix A.

The representative formulated product for the evaluation was 'Proquinazid 200 g/L EC', an emulsifiable concentrate (EC), containing 200 g/L proquinazid, registered under different trade names in the EU.

There is no agreed technical specification at the moment.

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 is possible.

Adequate methods are available to monitor all compounds given in the respective residue definition in food/feed of plant origin and environmental matrices. However, if MRLs will be set in food of animal origin according to the proposed residue definition for monitoring, an analytical method for the determination of the compounds of the residue definition will be required.

In mammals, proquinazid is of low acute toxicity to rats following oral, dermal or inhalation exposure; it is not a skin or eye irritant nor a skin sensitiser. The relevant short term toxicity NOAELs are 2 mg/kg bw/day in rat (based on altered thyroid homeostasis and associated follicular cell hypertrophy) and <15 mg/kg bw/day in the dog (increased incidence of clear ocular discharge). Proquinazid did not show any genotoxic potential. The relevant NOAEL for long term toxicity is 1.2 mg/kg bw/day from the rat study, based on thyroid and hepatic hyperplasia. Proquinazid was proposed for classification as **R40 "Limited evidence of a carcinogenic effect"** based on increased incidence of hepatocellular adenomas in rats (equivocal evidence in mice) and also an increased incidence of intestinal-type cholangiocarcinomas in rats. Both tumours were considered of limited relevance for human risk assessment. Proquinazid did not cause substance-related effects on reproductive parameters or organs in adult rats. The parental and reproductive NOAELs are 2 mg/kg bw/day and 35 mg/kg bw/day respectively. The offspring NOAEL is 11 mg/kg bw/day based on reduced litter weight. Proquinazid is not a developmental toxicant. The maternal and developmental NOAELs are 30 mg/kg bw/day (rat) and 2.5 mg/kg bw/day (rabbit), respectively. Proquinazid is not neurotoxic. The Acceptable Daily Intake (ADI) is 0.01 mg/kg bw/day based on the NOAEL from the 2-year study in rat, with a safety factor of 100; the Acute Reference Dose (ARfD) is 0.2 mg/kg bw (from the 90-day oral study in dog, SF 100) and the Acceptable Operator Exposure Level (AOEL) is

0.02 mg/kg bw (90-day oral study in rat, SF 100). The operator exposure to proquinazid is below the AOEL even without PPE (for the German model only), as well as for workers and bystanders.

Metabolism of proquinazid was investigated in grapes and in wheat under outdoor field conditions. Based on the available data, the main metabolic reactions in the metabolism of proquinazid in wheat plants and grapes could be established. The significant residues in the various wheat fractions were proquinazid and the metabolite IN-MW977[37] that was a major metabolite. In/on grape berries, proquinazid was only slowly metabolised to form minor amounts of IN-MM671[38] and IN-MM991[39]. Thus, the overall picture of metabolism was found to be slightly different in wheat and grapes. To confirm the identity of a significant unextractable fraction as lignin, a metabolism study in apples was evaluated in an addendum but not peer reviewed.

The proposed residue definition for consumer risk assessment for cereals and grapes is proquinazid and metabolite IN-MW977. Since the toxicological reference values of proquinazid can be applied to metabolite IN-MW977, residues of proquinazid and metabolite IN-MW977 should be expressed as proquinazid.

The proposed residue definition for plant products for enforcement monitoring for cereals and grapes is proquinazid alone. A conversion factor of 2 was established for cereals and of 1 for grapes as IN-MW977 was not formed in grapes.

A sufficient number of supervised residue trials are available in Northern and Southern Europe to support the representative uses on cereals and on grapes. The residue levels obtained in both Northern Europe and Southern Europe were similar. MRLs could be proposed for the different cereal crops barley, rye wheat, oats, triticale and for grapes. The trials are supported by valid storage stability data and validated analytical methods.

In a rotational crop study significant total residues were detected in feed items, e.g. soybean straw and wheat forage and straw, while residues were <0.01 mg/kg in crop parts for human consumption. The experts in PRAPeR 70 considered in particular that metabolite IN-MM671 is very persistent in soil and that it may accumulate in soil. Further assessment by the RMS was required, but the evaluation provided is not peer reviewed. Therefore a final peer reviewed conclusion on whether significant amounts of metabolites may be expected in succeeding crops (mainly feed items) could not be drawn.

The metabolism and distribution of proquinazid was investigated in goats and in hen. Exposure to goats is significant. It was agreed that the following residue definition in animal matrices should be proposed for risk assessment: Sum of proquinazid and metabolites IN-MU210[40] and IN-MW977 expressed as proquinazid. It was further agreed that for monitoring, the following residue definition in animal matrices should be proposed: Sum of proquinazid and metabolite IN-MU210, expressed as proquinazid. Residues are not expected to exceed 0.01 mg/kg in animal products, considering the animal intake from the notified representative uses, however risk managers may consider to set MRLs for a fat-soluble residue in food of animal origin on the LOQ of the analytical method for monitoring.

In a consumer risk assessment it could be demonstrated that chronic and acute dietary intake of a range of consumer groups is well below the toxicological reference values ADI and ARfD, respectively.

In the laboratory studies, proquinazid exhibits moderate to high persistence in soil under aerobic conditions at 20 ºC (DT50 lab 20 ºC = 39.5 – 345 d). The only major metabolite was IN-MM671

[37] IN-MW977: 2-{[(2*RS*)-2-hydroxypropyl]oxy}-6-iodo-3-propylquinazolin-4(3*H*)-one
[38] IN-MM671: 2-propoxy-3-propylquinazolin-4(3*H*)-one
[39] IN-MM991: 3-propylquinazoline-2,4(1*H*,3*H*)-dione
[40] IN-MU210: 3-[(6-iodo-4-oxo-3-propyl-3,4-dihydroquinazolin-2-yl)oxy]propanoic acid

(max 65 % AR after 120 d). This metabolite is highly persistent in soil under aerobic conditions in the study performed with the parent compound (DT50 lab 20 ºC = 170 – 305 d). In a separated study were it is applied as parent it is medium persistent in soil (DT50 lab 20 ºC = 71 – 94 d). Another metabolite, IN-MM991 (max. 7 % AR after 210 d) was observed in one of the soils at levels above 5 % AR in two consecutive sampling dates and therefore was assessed for potential ground water contamination. This metabolite is moderately persistent in soil (DT50 lab 20 ºC = 21 – 30 d). Metabolite IN-MM986 was also observed as a minor metabolite in soil (max. 8 % AR after 183 d). Also this metabolite is moderately persistent in soil (DT50 lab 20 ºC = 16 - 36 d). Mineralization was negligible in one of the soils and reached maximum levels of 2 – 28 % AR after 365 d in the other three soils. Unextractable residues at the end of the study (1 yr) reached levels between 15 – 32 % AR.

A water/sediment study under dark anaerobic conditions was provided as surrogate of the soil anaerobic study. Proquinazid exhibits medium persistence in this study (DT50 = 61 d). The same metabolites identified under aerobic conditions were found. Unextractable residues in the sediment amounted to 22.6 % AR at the end of the study (1 yr). No significant mineralization was observed under these conditions (1.3 % AR as CO_2 after 365 d).

Degradation of proquinazid was significantly enhanced by the irradiation of a light source simulating midday June sunlight in Phoenix, Arizona (DT50 = 19 d of continuous irradiation, corrected for degradation in the dark control; USA, Latitude 33º26' N). Metabolite IN-MM671 was the main metabolite (max. 14.45 % AR after 168 h of continuous irradiation).

Dissipation of proquinazid was investigated in four field dissipation studies in a total of eight European sites (2 in UK, 2 in Northern France, 2 in Southern France, 1 in Italy, 1 in Germany). Proquinazid 14C labelled at the phenyl ring was applied in one of the studies (Alconbury, UK). In the other sites, it was applied as emulsifiable concentrate formulations containing non labelled proquinazid and DPX-KZ165 (a substance under development at the time of the study that has not been commercialized). The metabolites IN-MM671, IN-MM991 and IN-MM986 appeared at levels above 10 % AR at various sampling points in the radiolabelled study. In non radiolabelled trials, only IN-MM671 and IN-MM986 were found consistently above 10 % of applied amount. All field dissipation trials were performed on bare soil, therefore contribution of photolysis to certain extend may not be excluded. In these trials, proquinazid was low to medium persistent in soil (DissT50 = 5 – 70 d), IN-MM671 was moderate to very highly persistent in soil (DissT50 = 29 – 394 d), IN-MM986 was moderately to medium persistent (DissT50 = 34 – 68.5 d) and IN-MM991moderately persistent to high persistent (DissT50 = 54 -104 d).

According to the results of the batch adsorption desorption studies proquinazid may be considered immobile in soil (Koc = 9091 – 16769 mL/g), IN-MM671 slightly mobile (Koc = 2333 - 4167 mL/g), IN-MM991 medium to highly mobile (Koc = 137 - 342 mL/g) and IN-MM986 slightly to low mobile (Koc = 1368 - 2500 mL/g) in soil.

Proquinazid and all the metabolites investigated were stable to hydrolysis (pH 4, 7 and 9; at 20 o C). In the aqueous photolysis study proquinazid is rapidly photolysed (DT50 < 1 h). Major photolysis metabolites identified were IN-MM671 (max. 17.2 % AR after 4h), IN-MM991 (max. 14.2 % AR after 1 h), IN-MM986 (max. 14.5 % AR after 2 h) and IN-MT884 (max. 30.5 % AR after 1d). Theoretical photolysis half-lives of proquinazid and its metabolites in the top layer (0.001cm) of an aqueous system integrated over a full day summer at 40 o latitude were calculated based on the results of this study.

According to the available study, proquinazid is not readily biodegradable.

In water / sediment systems, proquinazid partitioned rapidly into the sediment (DissT50 < 1 d). However, it is moderately to highly persistent in the total system (DT50 = 36.5 – 136 d). The only

metabolite identified was IN-MM671 (max 68 % AR in the sediment after 100 d, end of the study) that is very highly persistent in both systems (DT50 > 500 d). However this metabolite is strongly absorbed to the sediment and only amounts up to 6 % AR (after 30 d) are found in the water phase. Mineralization was practically negligible (CO2 0.2 - 1.4 % AR) and unextracted residues in the sediment ranged between values of 5 to 15 % AR.

PEC_{SW} were calculated by the applicant following FOCUS SW scheme. Step 1 and 2 were calculated for metabolites IN-MM986, IN-MM991 and IN-MT884. FOCUS SW Step 3 was calculated for proquinazid and metabolite IN-MM671. The RMS recalculated Step 3 with more adequate application windows. Since spray drift is deemed to be the main route of entry of proquinazid in surface water FOCUS Step 3 calculations were performed using both multiple and single application spray drift inputs. The applicant also provided FOCUS Step 4 calculations by introducing spray buffer zones of 3 m for cereals and 14 m for grapes. The RMS recalculated the FOCUS Step 4 for single and multiple applications with more adequate application dates. In the case of three out of the six late vines scenarios (single application) risk assessment failed with the 14 m buffer zone and the 16 m buffer zone was also calculated.

Potential groundwater contamination by proquinazid and its main soil metabolites was addressed with FOCUS GW PELMO 3.3.2. Concentration of proquinazid and metabolites IN-MM671, IN-MM991 and IN-MM986 was < 0.001 µg / L for all the uses and scenarios simulated.

Proquinazid has a vapour pressure of 9 x 10-5 Pa (25 ^{o}C) and a calculated Henry's Law constant of 3 x 10^{-2} Pa·m^3/mol. No atmospheric long range transport is expected for proquinazid because the calculated half-life for photochemical oxidative degradation in the atmosphere was calculated to be 4 h.

Tier I assessment provided TER values above the Annex VI trigger values for the acute and short-term risk to birds. The long-term TERs values were above the Annex VI trigger value for insectivorous and herbivorous birds for the use in cereals, whereas the TER for insectivorous birds for the use in vine failed to meet the trigger. The potential long-term risk for insectivorous birds in vine was refined by considering Yellowhammer (*Emberiza citronella*) and Cirl bunting (*Emberiza cirlus*), and their respective diets, as focal species. A mean of the 'Residue unit dose' for small and large insects was used and the resulted TERlt for insectivorous birds was above the trigger values. The acute and long-term risk to mammals was considered to be low.

The most likely exposure route for the metabolites would be through ingestion of contaminated earthworms or fish. Just the parent proquinazid and the metabolite IN-MM671 were considered for the assessment of secondary poisoning of earthworm- and fish-eating birds and mammals. Risk to birds and mammals from earthworm- and fish-eating birds and mammals for cereals, was considered to be low. The high risk identified for the fish-eating birds for vine was refined using the 21 days TWA PECsw from FOCUSsw step 3. With the available information the risk for the earthworm-eating birds following the use of proquinazid in vines could not be considered as low. The risk from uptake of contaminated water was considered to be low.

Proquinazid was considered to be very toxic to aquatic organisms. The acute risk to aquatic organisms was addressed at FOCUSsw step 2, without risk mitigation for the use in cereals. Risk mitigation measures equivalent to a 5 m non-spray buffer zone were needed to address the acute risk to aquatic organism in vines. For the long-term, TER values were below the Annex VI trigger values. FOCUS Step 4 calculations showed that non-spray buffer zones of 3 and 16 m for the use of proquinazid in cereals and vine respectively are necessary to protect the aquatic environment in the worst case scenarios. The risk of the relevant metabolites (IN-MM671, IN-MM986, IN-MM991) to aquatic organisms was considered to be low.

The risk to bees, non-target arthropods, earthworms, soil non-target micro-organisms and biological methods of sewage treatment was assessed as low.

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

- A 16 m non-spray buffer zone is necessary to protect the aquatic organisms for the representative use in vines. (See section 5.2).
- A 3 m non-spray buffer zone is necessary to protect the aquatic organisms for the representative use in cereals. (See section 5.2).

ISSUES THAT COULD NOT BE FINALISED

- The technical material specification.
- The evaluation of the expected amounts of residues in some rotational crops.
- Based on the available data it was not possible to address the risk to earthworm-eating birds from the intended use in vines.

CRITICAL AREAS OF CONCERN

- None.

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APPENDICES

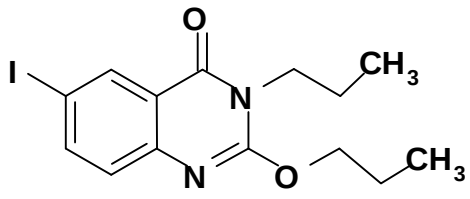
A. LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

Active substance (ISO Common Name) ‡	Proquinazid
Function (*e.g.* fungicide)	Fungicide

Rapporteur Member State	UK
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	6-iodo-2-propoxy-3-propylquinazolin-4(3*H*)-one
Chemical name (CA) ‡	6-iodo-2-propoxy-3-propyl-4(3*H*)-quinazolinone
CIPAC No ‡	764
CAS No ‡	189278-12-4
EC No (EINECS or ELINCS) ‡	None
FAO Specification (including year of publication) ‡	None
Minimum purity of the active substance as manufactured ‡	Open
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	$C_{14}H_{17}IN_2O_2$
Molecular mass ‡	372.21 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	61.5 °C – 62 °C (99.2%)
Boiling point (state purity) ‡	Not observed at temperatures below 360°C (99.6%)
Temperature of decomposition (state purity)	Thermal decomposition occurred at 367 °C (99.6%)
Appearance (state purity) ‡	White crystalline solid (99.2%)
Vapour pressure (state temperature, state purity) ‡	9×10^{-5} Pa at 25 °C (99.2%)
Henry's law constant ‡	3×10^{-2} Pa m^3 mol^{-1} at 25 °C
Solubility in water (state temperature, state purity and pH) ‡	Water solubility determined at 25 °C (99.5% purity): 0.97 mg/l HPLC grade water 0.93 mg/l pH 7 phosphate buffer 0.73 mg/l sea water *(solubility was stated to be unaffected by pH)*
Solubility in organic solvents ‡ (state temperature, state purity)	Solubilities at 25°C (99.5% purity): Acetone >250 g/kg Acetonitrile 154 g/l Dichloromethane >250 g/kg Dimethylformamide >250 g/kg Ethyl acetate >250 g/kg n-hexane >250 g/kg methanol 136 g/l 1-octanol >250 g/kg o-*xylene* *>250 g/kg*
Surface tension ‡ (state concentration and temperature, state purity)	73.9 mN/m for a saturated solution at 19.8°C (98%)
Partition co-efficient ‡ (state temperature, pH and purity)	Log K_{OW} = 5.5 at 25°C. pH not investigated as proquinazid does not dissociate between pH 2.4 and 11.6. *Indicates the potential to bioaccumulate.*
Dissociation constant (state purity) ‡	Not relevant. No dissociation between pH 2.4 and 11.6
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	98% purity, 12 and 19 ug/ml solutions: λ_{max} = 270 nm; ε = 1.6×10^4 $L.mol^{-1}.cm^{-1}$ at λ > 290 nm: λ_{max} = 325 nm; ε = 3×10^3 $L.mol^{-1}.cm^{-1}$ *The values obtained were consistent across pH 2,7 and 10.*

Flammability ‡ (state purity)	Not highly flammable (97%)
Explosive properties ‡ (state purity)	Non-explosive (97%)
Oxidising properties ‡ (state purity)	Non-oxidising (case based on structure)

Summary of representative uses evaluated (proquinazid)*

CROP and /or situation	Member State or Country	Product name	F G or I	Pest or group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of a.s. (g/L)	method kind	growth stage & season	number min max	interval between applications (min)	g a.s./hL min max	water L/ha min max	g a.s./ha min max		
W. Wheat S. Wheat	France Germany Ireland UK	Talendo, Talius	F	*Blumeria graminis*	EC	200	Hydraulic sprayer overall	BBCH 25 to BBCH 65 Spring	1-2	14 days	N/A	100-500	50 (max 100/ season)		Single application rate = 50 g a.s./ha
W. Barley S. Barley W. Rye Oats Triticale	France Germany Ireland UK	Talendo, Talius	F	*Blumeria graminis*	EC	200	Hydraulic sprayer overall	BBCH 25 to BBCH 49 Spring	1-2	14 days	N/A	100-500	50 (max 100/ season)		Single application rate = 50 g a.s./ha
Grapes	France	Talendo, Talius	F	*Uncinula necator*	EC	200	Air-blast atomizer or hydraulic sprayer with air-assistance	BBCH 13 to 28 DBH Spring /summer	1-4	14 days	33 - 17 g/hL	150-300	50 (max 200/ season)	28	Low volume application is French specific use.

CROP and /or situation	Member State or Country	Product name	F G or I	Pest or group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of a.s. (g/L)	method kind	growth stage & season	number min max	interval between applications (min)	g a.s./hL min max	water L/ha min max	g a.s./ha min max		
Grapes	Italy	Talendo, Talius	F	*Uncinula necator*	EC	200	Hydraulic sprayer with or without air assistance	BBCH 13 to 28 DBH Spring /summer	1-4	14 days	5.0 g as/hL	300-1500	15 - 75 (max 300/ season)	28	Maximum application rate by growth stage BBCH GS 13-61; 40 g a.s./ha BBCH GS 61-71; 60 g a.s./ha BBCH GS 71-28 days before harvest; 75 g a.s./ha Risk for earthworm-eating birds not covered by refinement application scheme

CROP and /or situation	Member State or Country	Product name	F G or I	Pest or group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of a.s. (g/L)	method kind	growth stage & season	number min max	interval between applications (min)	g a.s./hL max min	water L/ha min max	g a.s./ha min max		
Grapes	Spain	Talendo, Talius	F	*Uncinula necator*	EC	200	Hydraulic sprayer with or without air assistance	BBCH 13 to 28 DBH Spring /summer	1-4	14 days	5 g/hL	300-1000	15 - 50 (max 200/ season)	28	
Grapes	Portugal	Talendo, Talius	F	*Uncinula necator*	EC	200	Hydraulic sprayer with or without air assistance	BBCH 13 to 28 DBH Spring /summer	1-4	14 days	5 g/hL	300-1000	15 - 50 (max 200/ season)	28	

CROP and /or situation	Member State or Country	Product name	F G or I	Pest or group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of a.s. (g/L)	method kind	growth stage & season	number min max	interval between applications (min)	g a.s./hL max min	water L/ha min max	g a.s./ha min max		
Grapes	Greece	Talendo, Talius	F	*Uncinula necator*	EC	200	Hydraulic sprayer with or without air assistance	BBCH 13 to 28 DBH Spring /summer	1-4	14 days	5.0 g as/hL	300-1500	15 - 75 (max 300/ season)	28	Maximum application rate by growth stage BBCH GS 13-61; 25 g a.s./ha BBCH GS 61-71; 40 g a.s./ha BBCH GS 71-28 days before harvest; 75 g a.s./ha Risk for earthworm-eating birds not covered by refinement application scheme

CROP and /or situation	Member State or Country	Product name	F G or I	Pest or group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
					Type	Conc. of a.s. (g/L)	method kind	growth stage & season	number min max	interval between applications (min)	g a.s./hL min max	water L/ha min max	g a.s./ha min max		
Grapes	Germany	Talendo, Talius	F	*Uncinula necator*	EC	200	Hydraulic sprayer with or without air assistance	BBCH 13 to 28 DBH Spring /summer	1-4	14 days	5.0 g as/hL	400-1500	20 - 75 (max 300/ season)	28	Maximum application rate by growth stage BBCH GS 13-61; 40 g a.s./ha BBCH GS 61-71; 60 g a.s./ha BBCH GS 71-28 days before harvest; 75 g a.s./ha Risk for earthworm-eating birds not covered by refinement application scheme

∗ For uses where the column "Remarks" is marked in grey further consideration is necessary.

(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

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	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

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

Technical as (analytical technique)	Proquinazid in technical material was determined by HPLC with UV detection at 250nm.
Impurities in technical as (analytical technique)	Organic impurities in technical material were determined by HPLC with UV detection at 230nm. Residual solvents were determined by GC-FID.
Plant protection product (analytical technique)	Proquinazid in plant protection products was determined by GC-FID

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Proquinazid
Food of animal origin		Sum of proquinazid and metabolite IN-MU210 expressed as proquinazid
Soil		Proquinazid , IN-MM986, IN-MM671, and IN-MM991
Water	surface	Proquinazid , IN-MM986, IN-MM671, and IN-MM991
	drinking/ground	Proquinazid , IN-MM986, IN-MM671, and IN-MM991
Air		Proquinazid

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Proquinazid was determined by the modified multi residue method S19. Detection was by GC/MS with quantification on the ion m/z 288. LOQs were 0.01 mg/kg for apple, grape and wheat grain; 0.02 mg/kg for oilseed rape; 0.1 mg/kg for wheat straw.
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Proquinazid : modified multi residues method S19, with a LOQ of 0.02 mg/kg for meat and milk. Detection by GC/MS with quantification on the m/z 288 ion. Open (for metabolite IN-MU210)
Soil (analytical technique and LOQ)	Proquinazid and the metabolites IN-MM986, IN-MM671 and IN-MM991 were determined by GC/MS. The LOQ was 0.005 mg/kg for each compound. Quantification was on the m/z 288 ion for proquinazid and IN-MM986, and m/z 162 for IN-MM671 and IN-MM991.

Water (analytical technique and LOQ)	Proquinazid and the metabolites IN-MM986, IN-MM671 and IN-MM991 were determined in surface, ground and drinking water by GC/MS. The LOQ was 0.10 µg/L for each compound. Quantification was on the m/z 288 ion for proquinazid and IN-MM986, and m/z 162 for IN-MM671 and IN-MM991.
Air (analytical technique and LOQ)	Proquinazid was determined by GC-MS with the sum of the ions m/z 272, 288 and 330 being used for quantification, and an LOQ of 0.8 µg/m^3
Body fluids and tissues (analytical technique and LOQ)	Not required as proquinazid 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 ‡	83-84% within 24h (c. 60% in bile, c. 20% in urine) in biliary cannulation experiment
Distribution ‡	Widely distributed. At plasma Tmax (ie at 5-7h) after a single oral dose of 1mg/kg bw, highest levels in liver, kidneys, adrenal and fat. Similar findings 4-6h after the last of 7 daily doses of 1 mg/kg bw
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	Rapid and extensive at 1 and 20 mg/kg bw (85-88 % of dose within 48 h; 43-56% of dose in urine and 31-43% dose in faeces within 48h). Biliary excretion was extensive.
Metabolism in animals ‡	Extensively metabolised (> 98 %); the major metabolic reactions were phenyl ring hydroxylation and hydroxylation at the propyl and propoxy side chains, as well as some hydrolysis of side chains
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and metabolites
Toxicologically relevant compounds ‡ (environment)	No metabolites are predicted to occur in ground water at > 0.1 µg/l No impurities appear to be of clear toxicological concern.

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	4846 mg/kg bw	
Rat LD_{50} dermal ‡	> 5000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 5.2 mg/l air /4h (nose only exposure to proquinazid as airborne dust)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant	
Skin sensitisation ‡	Non-sensitiser (Magnusson and Kligman)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Thyroid (hypertrophy and hormone changes): rat Increased liver weight and ocular discharge: dog	
Relevant oral NOAEL ‡	90d rat: 30 ppm (2 mg/kg bw/d) 1y dog: <15 mg/kg bw/d	

6.6.5. ***Relevant dermal NOAEL ‡***	100 mg/kg bw/d (for systemic effects) Local dermal effects at 1000 mg/kg bw/d	
Relevant inhalation NOAEL ‡	No data - not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

Proquinazid is unlikely to be genotoxic	

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

Target/critical effect ‡	Liver (lesions); rats and mice Thyroid (hypertrophy, hyperplasia, hormone changes); rats	
Relevant NOAEL ‡	2y rat: 30 ppm (1.2 mg/kg bw/d)	
Carcinogenicity ‡	Thyroid: follicular cell adenoma in rat (equivocal evidence in mice). Not relevant for human health because a) rodents are more sensitive to this type of tumour induced by perturbation of thyroid hormone axis and b) proquinazid was of low potency for causing this tumour in rodents. Liver : hepatocellular adenoma in rats (equivoval evidence in mice) and a rat lesion termed “cholangiocarcinoma” (but which may not be neoplastic). These tumours/possible tumours are not considered to pose a carcinogenic risk to humans because they were seen in rats at doses above the MTD, ie in presence of marked liver and systemic toxicity. There are plausible non-genotoxic mechanisms for these tumours/possible tumours of the liver.	R40

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Marginal reduction in litter weight during lactation in presence of maternal toxicity	
Relevant parental NOAEL ‡	30 ppm = 2 mg/kg bw/d (thyroid)	
Relevant reproductive NOAEL ‡	600 ppm = 35-44 mg/kg bw/day (no adverse effects)	
Relevant offspring NOAEL ‡	150 ppm = 11 mg/kg bw/day (reduced litter weight)	

Developmental toxicity

Developmental target / critical effect ‡	Rat and rabbit: decreased fetal weight in presence of maternal toxicity	
Relevant maternal NOAEL ‡	Rat: 30 mg/kg bw/d (decreased body weight gain and food consumption; clinical signs) Rabbit: 2.5 mg/kg bw/d (decreased body weight gain and food consumption)	
Relevant developmental NOAEL ‡	Rat: 30 mg/kg bw/d (decreased fetal weight, delayed development) Rabbit: 2.5 mg/kg bw/d (decreased fetal weight)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	Rats: transient decrease in motor activity. This may reflect systemic toxicity rather than a primary effect on the nervous system. NOAEL 50 mg/kg bw.	
Repeated neurotoxicity ‡	Subchronic neurotoxicity, rats: NOAEL 600 ppm (50 mg/kg bw/d) = highest dose tested.	
Delayed neurotoxicity ‡	No data-not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	<u>Study of mechanism of thyroid effects in rats</u> Proposed mechanism based on study findings: induction of hepatic UDP-GT, leading to increased clearance of thyroid hormones, then increased serum TSH and thyroid hypertrophy (and ultimately tumours). Inhibition of hepatic 5'-deiodinase also reduces T3 and increases TSH. Thyroid changes (hypertrophy and hormones) and liver hypertrophy after exposure for 4 weeks were reversible.
Studies performed on metabolites or impurities ‡	<u>Toxicity of metabolite IN-MM671</u> Rat oral LD50 >2000 mg/kg bw, Ames negative, in vivo mouse bone marrow micronucIeus negative

Medical data ‡ (Annex IIA, point 5.9)

Limited information available since this is a new pesticide. No detrimental effects on health in manufacturing personnel

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw*	rat, 2y study	100
AOEL ‡	0.02 mg/kg bw/d	rat, 90d study	100 No correction for oral absorption
ARfD ‡	0.2 mg/kg bw*	Dog, 90d study (based on minimal acute effect, ocular discharge, at 19 mg/kg bw)	100

* The ADI and ARfD for proquinazid are also considered applicable to the metabolite IN-MW977 (a residue in grain)

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (e.g. name 50 % EC)	Proquinazid 200 g/l EC (the product tested): 2% (concentrate) and 12% (aqueous dilution). Determined from *in vivo* rat data, and *in vitro* data for rat and human skin

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Exposure estimates using the German model indicate the use of 'Proquinazid 200 g/L EC' on cereals or grapes is likely to result in a level of exposure to proquinazid within the AOEL where no PPE are worn. UK POEM (incorporating EUROPOEM data) suggests levels of exposure within the AOEL where PPE are worn'
Workers	Estimates of exposure predicted for workers entering grape or cereal crops treated with 'Proquinazid 200 g/L EC' indicate levels of exposure will be within the AOEL.

Bystanders	Estimates of exposure for bystanders exposed to 'Proquinazid 200 g/L EC' during spraying indicate levels of exposure will be within the AOEL.

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

	RMS/peer review proposal
Substance classified (name)	R40 (limited evidence of a carcinogenic effect)

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

Plant groups covered	Cereals (wheat) and fruiting crop (grapes)
Rotational crops	oilseeds (oilseed rape, soybean), root crop (sugar beet), cereals (wheat)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes; tentative analysis indicates that additional metabolites were present in following crops
Processed commodities	Proquinazid is hydrolytically stable under representative processing conditions
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	Proquinazid
Plant residue definition for risk assessment	Proquinazid and the metabolite 2-(2-Hydroxypropoxy)-6-iodo-3-propyl-4*(3H)*-quinazolinone (IN-MW977) and its isomer (also called IN-MW977). [the metabolite IN-MW977 and its isomer are not analytically distinguishable]
Conversion factor (monitoring to risk assessment)	For cereals a conversion factor of 2 is proposed to account for residues of the metabolite IN-MW977 which are present at the equivalent level to parent in the residue field trials. For grapes the factor should be 1 as metabolite IN-MW977 was not found in the grape metabolism study.

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

Animals covered	Ruminant (goat); poultry (hens)
Time needed to reach a plateau concentration in milk and eggs	Milk: 2-3 days (3 day study)
Animal residue definition for monitoring	sum of proquinazid and metabolite IN-MU210 expressed as proquinazid
Animal residue definition for risk assessment	sum of proquinazid and metabolites IN-MU210 and IN-MW977 expressed as proquinazid
Conversion factor (monitoring to risk assessment)	Non proposed; for assessed uses (cereals, grape) residues are not expected to exceed LOQ
Metabolism in rat and ruminant similar (yes/no)	yes
Fat soluble residue: (yes/no)	Yes; proquinazid (log Kow = 5.5)

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

A confined rotational crop study (3N) was conducted using phenyl-^{14}C (U) proquinazid. Low residue levels were detected in the straw/forage samples of soybean and wheat, however final peer reviewed conclusion on rotational crop residues is pending (note persistency of proquinazid and metabolite IN-MM671 in soil)

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

No significant decline in residues of proquinazid and IN-MW977 over eighteen months storage at ≤-18°C in wheat grain, forage and straw. No significant decline in residues of proquinazid and metabolite IN-MM671 (2-propoxy-3-propyl-4(*3H)*-quinazolinone) over nineteen months storage at ≤-18°C in grapes.

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	No	No
Potential for accumulation (yes/no):	Yes	Yes	N/A
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	N/A
	Feeding studies were not conducted. Metabolism data indicate that residues in animal products will not be significant		
Muscle	N/A	N/A	N/A
Liver	N/A	N/A	N/A
Kidney	N/A	N/A	N/A
Fat	N/A	N/A	N/A
Milk	N/A		
Eggs		N/A	

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 or Mediterranean Region, field or glasshouse, and any other useful information (a)	Trials results relevant to the representative uses	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Wheat Grain	N	Sum of total residues (proquinazid and IN-MW977): 5 x <0.02, 2 x <0.04, 1 x 0.04		0.05$^{\$}$ (proquinazid)	0.04	0.02
Wheat Straw	N	Sum of total residues (proquinazid and IN-MW977): 1 x 0.19, 1 x 0.27, 1 x 0.42, 1 x 0.57, 1 x 0.59, 1 x 0.72, 1 x 0.73 1 x 0.83			0.83	0.58
Wheat Grain	S	Sum of total residues (proquinazid and IN-MW977): 2 x <0.02, 4 x <0.04		0.05$^{\$}$ (proquinazid)	<0.04	0.04
Wheat Straw	S	Sum of total residues (proquinazid and IN-MW977): 1 x 0.46, 1 x 0.49, 1 x 0.51, 1 x 0.57, 1 x 0.73, 1 x 0.74			0.74	0.59
Barley, Rye, triticale and oats grain	N	Sum of total residues (proquinazid and IN-MW977): 13 x <0.04		0.05$^{\$}$ (proquinazid)	<0.04	0.04
Barley, Rye, triticale and oats straw	N	Sum of total residues (proquinazid and IN-MW977): 1 x 0.11, 2 x <0.2, 1 x 0.22, 1 x 0.23, 3 x 0.25, 1 x 0.31, 1 x 0.66, 1 x 0.75, 1 x 0.79, 1 x 0.85			0.85	0.25
Barley, Rye, triticale and oats grain	S	Sum of total residues (proquinazid and IN-MW977): 1 x 0.02, 1 x		0.05$^{\$}$ (proquinazid)	<0.04	0.04

		0.04, 7 x <0.04				
Barley, Rye, triticale and oats straw	S	Sum of total residues (proquinazid and IN-MW977): 1 x 0.20, 1 x 0.26, 1 x 0.28, 1 x 0.29, 1 x 0.42, 1 x 0.48, 1 x 0.49, 1 x 0.51, 1 x 0.53			0.53	0.42
Grapes	N	Proquinazid: 2 x 0.07, 1 x 0.09, 1 x 0.11, 1 x 0.12, 1 x 0.14, 1 x 0.15, 1 x 0.16, 1 x 0.20, 1 x 0.21, 1 x 0.35		0.5 proquinazid	0.35	0.15
Grapes	S	Proquinazid: 1 x <0.02, 2 x 0.02, 1 x 0.04, 1 x 0.06, 2 x 0.09, 1 x 0.17, 1 x 0.19, 1 x 0.25, 1 x 0.35		0.5 proquinazid	0.35	0.07

(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

$ The MRLs proposed are for proquinazid in cereals and proquinazid only in grapes. A conversion factor of x2 is needed to conduct the risk assessment for cereals based on broadly equivalent residues of parent and the metabolite as seen in the residue trials.

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.01 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	0.000183 mg/kg bw/day (<2% ADI)
TMDI (% ADI) according to national (to be specified) diets	TMDI not calculated – instead the NEDI was calculated for the UK diet.
IEDI (WHO European Diet) (% ADI)	-
NEDI (specify diet) (% ADI)	UK diet: range from 0.00032 mg/kg bw/day (3% ADI) for elderly residential – 0.002175 mg/kg bw/day (22% ADI) for toddlers
Factors included in IEDI and NEDI	Grapes – processing factor for raisin and wine
ARfD	0.2 mg/kg bw/day
IESTI (% ARfD)	-
NESTI (% ARfD) according to national (to be specified) large portion consumption data	UK diet: Intakes for cereals range from <0.1 (various consumer groups) to 0.3% (infants, toddlers and 4-6 year olds) of the ARfD. Intake for table grapes range from 0.00733 mg/kg bw/day (3.7% ARfD) for elderly residential to 0.0555 mg/kg bw/day (27.8% ARfD) for toddlers. Intakes for wine range from 0.00027 mg/kg bw/day (0.1% ARfD) for various consumer groups to 0.0010 mg/kg bw/day (0.5% ARfD) for adults.
Factors included in IESTI and NESTI	Grapes – processing factor for raisin and wine

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Grapes/wine production/wine	4	0.2		
Grapes/drying/raisin	4	2.6		

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

.....	Wheat – 0.05 mg/kg Barley – 0.05 mg/kg Oats – 0.05 mg/kg Triticale – 0.05 mg/kg Rye – 0.05 mg/kg Grapes (table and wine) – 0.5 mg/kg

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.

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

Mineralization after 100 days ‡	0.1 – 10% AR at 120 - 122 days (n^{41}= 4)
Non-extractable residues after 100 days ‡	6 – 15% AR at 120 - 122 days (n = 4)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	IN-MM671: 27 – 65 % AR at 120 – 122 days (n=4) IN-MM986: 0.8 – 2 % AR at 60 – 120 days, max 8 % at 183 d (n=4); > 10 % AR in the radiolabelled field study. IN-MM991: 1 – 7 % AR at 120 – 122 days (n=4); > 10 % AR in the radiolabelled field study.

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

Anaerobic degradation ‡

Mineralization after 100 days	0.56% AR at 120 days (n=1)
Non-extractable residues after 100 days	14.1% AR at 120 days (n= 1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	IN-MM671 45.25% AR at 120 days (n=1) IN-MM986 0.23% AR at 120 days (n=1) IN-MM991 1.21% AR at 120 days (n=1)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	Mineralisation <1% AR at 15 days (dark control <1% AR at 15 days); (n=1) Unextracted residues 40.4% AR at 15 days (dark control 6.67% AR at 15 days) ; (n=1) Metabolites: IN-MM 671 8.1% AR at 15 days (dark control 14.45% AR at 7 days) ; (n=1) Parent DT50 15.5 days under study conditions (dark control DT50 82 days). Parent DT50 corrected for dark control equivalent to 38 days midday June sunlight, Phoenix, Arizona, USA, assuming 12 hour light/dark periods.

[41] n corresponds to the number of soils.

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

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type (USDA)	X[42]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Arrow – Sandy Loam		6.0	20 °C/ 75 % of $^1/_3$ bar	345/ 1150	239	0.987	SFO – box model
Keyport – Silt Loam		5.5	20 °C/ 75 % of $^1/_3$ bar	58/ 192	41	0.963	SFO – box model
Nambsheim – Sandy Loam		7.3	20 °C/ 75 % of $^1/_3$ bar	39.5/ 131	28	0.953	SFO – box model
Speyer 2.2 – Loamy Sand		6.3	20 °C/ 75 % of $^1/_3$ bar	204/ 678	122	0.985	SFO – box model
*Nambsheim – Silt Loam		8.1	10 °C/ 40 – 50 % 0bar	79/ 263	24	0.911	SFO
Geometric mean			-	-	60	-	-

* The Nambsheim soil incubation at 10 °C was included because soil characteristics were significantly different from the Nambsheim soil used in the 20 °C study, even though the soils share the same name.

IN-MM671	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	*f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Nambsheim – Silt Loam		8.1	20°C at 40-50% of 0 bar	71/ 236	*-	47	0.688	SFO
Keyport – Loam		7.1	20°C at 40-50% of 0 bar	94/ 312	*-	62	0.830	SFO
Speyer – Sandy loam		5.7	20°C at 40-50% of 0 bar	92/ 306	*-	67	0.759	SFO
Keyport – Silt Loam		5.5	20 °C/ 75 % of $^1/_3$ bar	223/ 742	0.83	156	0.963	SFO –box model
Nambsheim – Sandy Loam		7.3	20 °C/ 75 % of $^1/_3$ bar	170/ 565	1.0	117	0.953	SFO – box model

[42] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

IN-MM671	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	*f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Geometric mean						~~54~~ 81		

* Formation fractions are not calculated as studies were conducted with metabolite applied to soil.
NB. Geomean is calculated treating all 5 data points as separate values since the Keyport and Nambsheim soils have different soil properties even though the soil names are the same for two separate studies.

IN-MM986	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Nambsheim – Silt Loam		8.1	20°C at 40-50% of 0 bar	16/ 52	*-	11	0.929	SFO
Keyport – Loam		7.1	20°C at 40-50% of 0 bar	21/ 69	*-	14	0.942	SFO
Speyer – Sandy loam		5.7	20°C at 40-50% of 0 bar	36/ 118	*-	26	0.720	SFO
Geometric mean						16		

* Formation fractions are not calculated as studies used applied metabolite

IN-MM991	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Nambsheim – Silt Loam		8.1	20°C at 40-50% of 0 bar	21/ 70	*-	14	0.900	SFO
Keyport – Loam†		7.1	20°C at 40-50% of 0 bar	76/ 253	*-	51†	0.629	SFO
Speyer – Sandy loam		5.7	20°C at 40-50% of 0 bar	30/ 98	*-	22	0.742	SFO
Maximum						22†		

* Formation fractions are not calculated as studies used applied metabolite
† The Keyport loam was not considered to provide an appropriate fit to inform an input parameter for FOCUS modelling. Therefore the longest DT50 value of 22 days should be used in modelling. It is not considered that this change will affect PEC values significantly.

Field studies ‡

Parent	Aerobic conditions								
Soil type (USDA unless stated otherwise).	Location (country or USA state).	X[1]	pH	Depth (cm)	$DissT_{50}$ (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) Norm *	Method of calculation
Clay Loam – Bare soil (SSEW classification)	Alconbury, UK		7.0	0 - 30	70	231	0.873	_	SFO – box model
Sandy Loam – Bare soil	Nambsheim, N. France		7.8	0 – 10	14	46	0.931	_	SFO – box model
Silty Clay – Bare soil	Le Thor, S. France		7.9	0 – 10	39	128	0.813	_	SFO – box model
Silt Loam – Bare soil	Asti, Italy		7.6	0 – 10	20	65	0.955	_	SFO – box model
Silty Clay Loam – Bare soil	Gebstedt, Germany		7.4	0 – 10	43	143	0.841	_	SFO – box model
Silt Clay Loam – Bare soil	Engenville, N. France		7.6	0 – 10	45	148	0.889	_	SFO – box model
Silt Loam – Bare soil	Pompignan, S. France		5.1	0 - 10	5.5	18	0.977	_	SFO – box model
Sandy Loam – Bare soil	Essex, UK		8.1	0 - 20	7.2	24	0.860	_	SFO – box model
Geometric mean/median								-	

* normalised DT50 values were not calculated as the assessment was conducted prior to FOCUS kinetics when normalised field values were not required. Due to the contribution of photolysis the values should be regarded as dissipation not only microbial or chemical degradation.

IN-MM671	Aerobic conditions								
Soil type (USDA unless stated otherwise).	Location	Max form-ation (% AR)	pH	Depth (cm)	$DissT_{50}$ (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.*	Method of calculation
Clay Loam – Bare soil (SSEW classification)	Alconbury, UK	31.8	7.0	0 - 30	304	1010	0.873	-	SFO/SFO – box model

IN-MM671	Aerobic conditions								
Soil type (USDA unless stated otherwise).	Location	Max form-ation (% AR)	pH	Depth (cm)	$DissT_{50}$ (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.*	Method of calculation
Sandy Loam – Bare soil	Nambsheim, N. France	14.9	7.8	0 – 10	194	643	0.931	-	SFO/SFO – box model
Silty Clay – Bare soil	Le Thor, S. France	13.9	7.9	0 – 10	394	1310	0.813	-	SFO/SFO – box model
Silt Loam – Bare soil	Asti, Italy	40.5	7.6	0 – 10	138	459	0.955	-	SFO/SFO – box model
Silty Clay Loam – Bare soil	Gebstedt, Germany	19.0	7.4	0 – 10	78	259	0.841	-	SFO/SFO – box model
Silt Loam – Bare soil	Pompignan, S. France	10.2	5.1	0 - 10	29	97	0.982	-	SFO/SFO – box model
Sandy Loam – Bare soil	Essex, UK	20.1	8.1	0 - 20	265	880	0.860	-	SFO/SFO – box model
Geometric mean/median								-	

* normalised DT50 values were not calculated as the assessment was conducted prior to FOCUS kinetics when normalised field values were not required.

IN-MM986	Aerobic conditions								
Soil type (USDA unless stated otherwise).	Location	Max form-ation (% AR)	pH	Depth (cm)	$DissT_{50}$ (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.*	Method of calculation
Clay Loam – Bare soil (SSEW classification)	Alconbury, UK	23.0	7.0	0 - 30	68.5	228	0.616	-	SFO/SFO – box model
Silty Clay – Bare soil	Le Thor, S. France	13.6	7.9	0 – 10	34	114	0.811	-	SFO/SFO – box model
Silt Loam – Bare soil	Pompignan, S. France	32.8	5.1	0 - 10	48	160	0.972	-	SFO/SFO – box model
Geometric mean/median								-	

* normalised DT50 values were not calculated as the assessment was conducted prior to FOCUS kinetics when normalised field values were not required.

IN-MM991	Aerobic conditions								
Soil type (USDA unless stated otherwise).	Location	Max form-ation (% AR)	pH	Depth (cm)	$DissT_{50}$ (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.*	Method of calculation
Clay Loam – Bare soil (SSEW classification)	Alconbury, UK	13.4	7.0	0 - 30	104	347	0.972 (χ^2 28.9)	-	SFO/SFO – box model
Silt Loam – Bare soil	Pompignan, S. France	8.6	5.1	0 - 10	54	180	0.972	-	SFO/SFO – box model
Geometric mean/median								-	

* normalised DT50 values were not calculated as the assessment was conducted prior to FOCUS kinetics when normalised field values were not required.

pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	No accumulation expected for proquinazid. The maximum accumulated PECsoil for IN-MM671 under vines use, assuming a maximum total dose of 300 g a.s./ha, 26.8% w/w formation and DT50 of 394 days, is 0.113 mg/kg. The 'steady state' concentration (i.e. concentration just before application) would be 0.06 mg/kg. These values would be obtained in the 14th year of application. The maximum accumulated PECsoil for IN-MM671 under cereals use, assuming a maximum total dose of 100 g a.s./ha and the same assumptions as detailed above, is 0.024 mg/kg. The 'steady state' concentration (i.e. concentration just before application) would be 0.006 mg/kg; these values would occur in the fourth year of application.

Laboratory studies ‡

Parent	Anaerobic conditions						
Soil type (USDA)	X[43]	pH	t. °C	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C	St. (r^2)	Method of calculation
Brandywine Creek, USA – sand (sediment)		6.5	20 °C	61/ 202	61/ 202	0.973	SFO
Geometric mean/median			-	-	-	-	-

[43] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type (USDA)	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Arrow – Sandy Loam	1.9	5.3	-	-	174	9091	0.92
Evesham 3 - Loam	1.7	7.1	-	-	200	11493	0.91
Nambsheim – Sandy Loam	0.6	7.3	-	-	107	16769	0.93
Speyer 2.2 – Loamy Sand	2.1	6.4	-	-	295	14126	0.98
Arithmetic mean					194	12870	0.94
pH dependence, Yes or No			No				

IN-MM671‡							
Soil Type (USDA)	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Nambsheim – Loam	0.64	8.0	-	-	14	2333	0.99
Speyer 2.2 – Sandy Loam	1.91	5.9	-	-	65	3421	1.18
Keyport – Silt Loam	1.22	5.2	-	-	50	4167	1.15
Arrow – Sandy Loam	1.51	6.2	-	-	49	3267	1.12
Arithmetic mean/median					45	3297	1.11
pH dependence (yes or no)			Yes. Decreasing Koc with increasing pH.				

IN-MM986 ‡							
Soil Type (USDA)	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Nambsheim – Loam	0.64	8.0	-	-	15	2500	0.87
Speyer 2.2 – Sandy Loam	1.91	5.9	-	-	26	1368	0.83
Keyport – Silt Loam	1.22	5.2	-	-	38	3167	1.08
Arrow – Sandy Loam	1.51	6.2	-	-	37	2467	0.99
Arithmetic mean/median					29	2376	0.94
pH dependence (yes or no)			No				

IN-MM991 ‡							
Soil Type (USDA)	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n

Nambsheim – Loam	0.64	8.0	-	-	1.5	250	0.78
Speyer 2.2 – Sandy Loam	1.91	5.9	-	-	2.6	137	0.79
Keyport – Silt Loam	1.22	5.2	-	-	4.1	342	0.83
Arrow – Sandy Loam	1.51	6.2	-	-	4.9	327	0.86
Arithmetic mean/median					3.3	264	0.82
pH dependence (yes or no)			No				

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

Column leaching ‡	Not submitted, not required.
Aged residues leaching ‡	Not submitted, not required.
Lysimeter/ field leaching studies ‡	Not submitted, not required.

PEC (soil) (Annex IIIA, point 9.1.3)

Proquinazid	DT_{50} (d): 70 days (realistic worst case from field studies)
Method of calculation	Kinetics: SFO
	Field or Lab: field studies.
Application data	Crop: vines and cereals
	Depth of soil layer: 5cm
	Soil bulk density: 1.5g/cm^3
	% plant interception: 50 % crop interception (both crops)
	Number of applications: 4 (vines); 2 (cereals)
	Interval (d): 14 d (both crops)
	Application rate(s): 75 g as/ha (vines); 50 g as/ ha (cereals)

Vines

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	-		0.164	
Short term 24h	-	-	0.163	0.164
2d	-	-	0.161	0.163
4d	-	-	0.158	0.161
Long term 7d	-	-	0.153	0.159
14d	-	-	0.143	0.154
28d	-	-	0.125	0.144
50d	-	-	0.100	0.130
100d	-	-	0.061	0.104

Cereals

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	-		0.062	
Short term 24h	-	-	0.062	0.062
2d	-	-	0.061	0.062
4d	-	-	0.060	0.061
Long term 7d	-	-	0.058	0.060
14d	-	-	0.054	0.058
28d	-	-	0.047	0.054
50d	-	-	0.038	0.049
100d	-	-	0.023	0.040

IN-MM671 Method of calculation	Maximum formation: 26.8% w/w observed formation from parent in field studies DT_{50} (d): 394 days (realistic worst case from field studies) Kinetics: SFO Field or Lab: Field studies.
Application data	Application rate assumed: Vines - Maximum total dose 300 g a.s./ha, 50% crop interception Cereals - Maximum total dose 100 g a.s./ha, 50% crop interception

Vines $PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	-		0.054	
Short term 24h	-	-	0.054	0.054
2d	-	-	0.053	0.054
4d	-	-	0.053	0.053
Long term 7d	-	-	0.053	0.053
21d	-	-	0.052	0.053
28d	-	-	0.051	0.052
50d	-	-	0.049	0.051
100d	-	-	0.045	0.049
Plateau concentration	The maximum accumulated PECsoil for IN-MM671 under vines use is 0.113 mg/kg. The 'steady state' concentration (i.e. concentration just before application) would be 0.06 mg/kg. These values would be obtained in the 14th year of application.			

Cereals PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	-		0.018	
Short term 24h	-	-	0.018	0.018
2d	-	-	0.018	0.018
4d	-	-	0.018	0.018
Long term 7d	-	-	0.018	0.018
21d	-	-	0.017	0.018
28d	-	-	0.017	0.017
50d	-	-	0.016	0.017
100d	-	-	0.015	0.016
Plateau concentration	The maximum accumulated PECsoil for IN-MM671 under cereals use, is 0.024 mg/kg. The 'steady state' concentration (i.e. concentration just before application) would be 0.006 mg/kg; these values would occur in the fourth year of application.			

IN-MM986 Method of calculation	Maximum formation: 29.1% w/w observed formation from parent in field studies DT_{50} (d): 69 days (realistic worst case from field studies) Kinetics: SFO Field or Lab: Field studies.
Application data	Application rate assumed: Vines - Maximum total dose 300 g a.s./ha, 50% crop interception Cereals - Maximum total dose 100 g a.s./ha, 50% crop interception

Vines $PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	-		0.058	
Short term 24h	-	-	0.058	0.058
2d	-	-	0.057	0.058
4d	-	-	0.056	0.057
Long term 7d	-	-	0.054	0.056
21d	-	-	0.051	0.054
28d	-	-	0.044	0.051
50d	-	-	0.035	0.046
100d	-	-	0.021	0.037

Cereals $PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	-		0.019	
Short term 24h	-	-	0.019	0.019
2d	-	-	0.019	0.019
4d	-	-	0.019	0.019
Long term 7d	-	-	0.018	0.019
21d	-	-	0.017	0.018
28d	-	-	0.015	0.017
50d	-	-	0.012	0.015
100d	-	-	0.007	0.012

IN-MM9991 Method of calculation	Maximum formation: 7.4 % w/w observed formation from parent in field studies DT_{50} (d): * Kinetics: SFO Field or Lab: Field studies.
Application data	Application rate assumed: Vines - Maximum total dose 300 g a.s./ha, 50% crop interception Cereals - Maximum total dose 100 g a.s./ha, 50% crop interception

Vines $PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	-		0.015	

Cereals $PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	-		0.005	

* DT50 value of 54 days and TWA values deleted because the DT50 value of 54 days used in the calculation was not the longest field DT50 value (following PRAPeR meeting consideration). However TWA values are not used in the risk assessment and therefore no new PECsoil TWA values are required for IN-MM991.

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 4, 20˚C: Proquinazid, IN-MM671, IN-MM986, IN-MM991 and IN-MM884 stable
	pH 7, 20˚C: Proquinazid, IN-MM671, IN-MM986, IN-MM991 and IN-MM884 stable
	pH 9, 20˚C: Proquinazid, IN-MM671, IN-MM986, IN-MM991 and IN-MM884 stable
Photolytic degradation of active substance and metabolites above 10 % ‡	Proquinazid DT_{50} : 0.03 d (dark control stable) Xenon lamp, wavelengths >290 nm only, 15 day duration, equivalent to 30 days midday natural sunlight in Ohio, USA (40 ˚N). IN-MM671: 19.5 % AR (0.21 d); DT50 = 5 d IN-MM986: 14.5 % AR (0.08 d); DT50 = 11 d IN-MM991: 14.2 % AR (0.04 d); DT50 = 4 d IN-MT884: 30.5 % AR (1 d); DT50 = 39 d Theoretical photolytic half-lives calculated by 'GCSolar' in top layer (0.002 cm) of an aqueous system integrated over a full day in summer at 40° latitude were: Proquinazid 0.3 days IN-MM671 16.1 days IN-MM986 32.8 days IN-MM991 12.7 days[44] IN-MT884 132 days[4]
Quantum yield of direct phototransformation in water at Σ > 290 nm	Proquinazid 0.00745 mol · Einstein $^{-1}$ IN-MM671 0.000075 mol · Einstein $^{-1}$ IN-MM986 0.0000195 mol · Einstein $^{-1}$ IN-MM991 0.00013 mol · Einstein $^{-1}$ IN-MT884 0.000137 mol · Einstein $^{-1}$
Readily biodegradable ‡ (yes/no)	No.

[44] Considered not fully reliable by the RMS

Degradation in water / sediment

Proquinazid	Distribution (max in water 26 – 33 % at 0 d. Max. sed 78 - 86 % after 3 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Middletown, USA – Red Oak Stream	7.5	7.3	20	136/ 453	0.683	0.82/ 2.71*	0.999	191/ 635	0.766	SFO
Middletown, USA, Town Park Pond	7.2	7.2	20	36.5/ 121	0.978	0.75/ 2.48*	0.999	38/ 125	0.939	SFO. Sequential box model for total system.
Geometric mean				70.5		0.78		85.2		

* Values represent dissipation rates NOT degradation rates

IN-MM671	Distribution (max in water 6 – 7 % AR after 15 – 60 d. Max. in sed 32 – 68% AR after 100 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Middletown, USA – Red Oak Stream	7.5	7.3	20	-	-	-	-	-	-	No reliable dissipation rates were calculable
Middletown, USA, Town Park Pond	7.2	7.2	20	-	-	-	-	-	-	No reliable dissipation rates were calculable
Geometric mean/median			-	-		-		-		-
IN-MM991	Distribution (Max. in sed 1.2 % AR after 60 d at Town Park. Not detected at Red Oak Stream)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Middletown, USA, Town Park Pond	7.2	7.2	20	-	-	-	-	-	-	Dissipation rates not calculable
Geometric mean/median			-	-		-		-		-

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
Middletown, USA – Red Oak Stream	7.5	7.3	1.4 % AR at 100 d (study end)	14.6 % AR at 3 d	7.0 % AR at 100 d (study end)
Middletown, USA, Town Park Pond	7.2	7.2	0.2 % AR at 100 d (study end)	12 % AR at 7 d	7.1 % AR at 100 d (study end)

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Proquinazid Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: Version 1.1 Molecular weight (g/mol): 372.2 Water solubility (mg/L): 0.93 K_{OC} (L/kg): 12870 (mean value) DT_{50} soil (d): 60 days (Geomean lab value) DT_{50} water/sediment system (d): 86 days (arithmetic mean from sediment water studies) DT_{50} water (d): 300 (default worst case according to aquatic assessment guidelines). DT_{50} sediment (d): 114.5 (arithmetic mean from water/sediment studies) Crop interception (%): average crop cover for vines and cereals (50 %)
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: SWASH v. 1.1, FOCUS MACRO v. 4.2.2, FOCUS PRZM v. 1.1, and FOCUS TOXSWA v. 1.1.1. Vapour pressure: 9×10^{-5} Pa (at 20º C) Koc (mL/g): 12870 1/n: 0.94 (Freundlich exponent general or for soil, susp. solids or sediment respectively)
Parameters used in FOCUSsw step 4 (if performed)	Step 4 calculations are also presented for winter cereals (3m buffer zone) and late vines (16m buffer zone) assuming single applications. Drift rates were: Cereals (3 m buffer): 0.9425 % Vines Late (16 m buffer): 0.7213 %
Application rate	Crop: Winter cereals, spring cereals, vines (early appl.), vines (late appl.).* Crop interception: 50 % (all crops) Number of applications: 2 (cereals); 4 (vines) Interval (d): 14 days Individual application rate(s): 50 g as/ha (cereals); 75 g as/ ha (vines) Application window: Step 1 & 2: Winter cereals – Northern Europe (March – May) Spring cereals – Northern Europe (March – May) Vines (early appl.) - Northern Europe (June - Sept) Vines (early appl.) - Southern Europe (March – May) Vines (late appl.) - Northern Europe (June - Sept)

Vines (late appl.) - Southern Europe (June - Sept)		
Application window: Step 3:		
Scenario	Winter cereals	Vines
D1	April 15th – May 31st	-
D2	April 1st – May 14th	-
D3	April 1st – May 14th	-
D4	March 15th – April 30th	-
D5	March 15th – April 30th	-
D6	March 1st – April 14th	April 1st – June 30th
R1	March 15th – April 30th	June 1st – Aug 31st
R2	-	April 15th – July 14th
R3	March 1st – April 14th	May 1st – July 31st
R4	March 1st – April 14th	May 1st – July 31st

* Risk assessments for sediment dwelling organisms finish at Step 2. At Step 3, the highest PECsw values are produced from calculations based on single application, but highest PECsed values at Step 3 are obtained from multiple applications. As the Step 3 PECsed values are not required for risk assessment, presentation of PECsw and PECsed are only from single applications. In addition, the highest PEC values for cereals were from winter crops, and for vines from late application. Thus PEC values are only presented for winter cereals and late vines. Note single application PEC values generated by modelling drainflow/runoff for multiple applications, but adding spray drift input appropriate for a single application for only the final application.

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Winter and Spring cereals	0 h	2.76		236.2	
	24 h	1.87	2.31	240.8	238.5
	2 d	1.86	2.09	238.9	239.2
	4 d	1.83	1.96	235.0	238.1
	7 d	1.78	1.90	229.4	235.6
	14 d	1.68	1.81	216.8	229.3
	21 d	1.59	1.76	205.0	223.2
	28 d	1.51	1.70	193.7	217.2
	42 d	1.34	1.61	173.0	205.9
	50 d	1.26	1.56	162.2	199.7
	100 d	0.84	1.30	108.4	166.6

The maximum water concentration at Step 1 for cereals based on the total load of proquinazid if this were to all be present in the in the water phase is 34.12 µg/l. This value is required for sediment dweller risk assessment.

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Vines (late appl.)	0 h	13.53		708.7	
	24 h	5.90	9.72	759.45	734.07
	2 d	5.85	7.80	753.35	745.24
	4 d	5.76	6.80	741.31	746.27
	7 d	5.62	6.33	723.60	740.34
	14 d	5.31	5.90	683.90	721.95
	21 d	5.02	5.65	646.39	702.96
	28 d	4.75	5.46	610.93	684.34
	42 d	4.24	5.14	545.74	648.80
	50 d	3.98	4.97	511.66	629.55
	100 d	2.66	4.12	341.95	525.34

The maximum water concentration at Step 1 for vines late application based on the total load of proquinazid if this were to all be present in the in the water phase is 107.60 µg/l. This value is required for sediment dweller risk assessment.

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Winter and Spring cereals Single Application Northern EU	0 h	0.46		14.38	
	24 h	0.17	0.31	14.30	14.34
	2 d	0.08	0.22	14.22	14.30
	4 d	0.13	0.15	14.06	14.22
	7 d	0.11	0.13	13.82	14.10
	14 d	0.11	0.12	13.27	13.82
	21 d	0.10	0.12	12.75	13.55
	28 d	0.10	0.11	12.24	13.28
	42 d	0.09	0.11	11.29	12.78
	50 d	0.09	0.10	10.79	12.50
	100 d	0.07	0.09	8.09	10.94
Winter and Spring Cereals Multiple Application Northern EU	0 h	0.44		26.14	
	24 h	0.18	0.31	26.00	26.07
	2 d	0.10	0.22	25.84	25.99
	4 d	0.23	0.17	25.55	25.85
	7 d	0.20	0.19	25.11	25.62
	14 d	0.19	0.19	24.12	25.12
	21 d	0.19	0.19	23.17	24.63
	28 d	0.18	0.19	22.25	24.15
	42 d	0.17	0.18	20.53	23.22
	50 d	0.16	0.18	19.60	22.72
	100 d	0.12	0.16	14.70	19.88

The maximum water concentration at Step 2 for cereals based on the total load of proquinazid if this were to all be present in the in the water phase is 3.74 µg/l. This value is required for sediment dweller risk assessment.

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Vines (late appl.) Single Application Southern EU	0 h	2.01		39.08	
	24 h	0.74	1.37	38.85	38.97
	2 d	0.34	0.96	38.63	38.85
	4 d	0.37	0.62	38.19	38.63
	7 d	0.30	0.49	37.53	38.30
	14 d	0.29	0.39	36.05	37.54
	21 d	0.28	0.36	34.63	36.81
	28 d	0.27	0.34	33.26	36.09
	42 d	0.25	0.31	30.68	34.71
	50 d	0.24	0.30	29.30	33.96
	100 d	0.18	0.25	21.97	29.71
Vines (late appl.) Multiple Application Southern EU	0 h	1.02		122.95	
	24 h	0.96	0.99	122.67	122.81
	2 d	0.95	0.97	121.96	122.56
	4 d	0.94	0.96	120.57	121.91
	7 d	0.93	0.95	118.50	120.89
	14 d	0.89	0.93	113.82	118.52
	21 d	0.85	0.91	109.32	116.20
	28 d	0.82	0.89	105.01	113.94
	42 d	0.76	0.86	96.87	109.59
	50 d	0.72	0.84	92.51	107.20
	100 d	0.54	0.73	69.37	93.79

The maximum water concentration at Step 2 for vines based on the total load of proquinazid if this were to all be present in the in the water phase is 17.98 µg/l; this is from late application in Southern Europe assuming applications during June - September. This value is required for sediment dweller risk assessment.

STEP 3

Summary of global maximum PEC_{SW} and PEC_{SED} of proquinazid from all drainage (D) and runoff (R) scenarios following the use of proquinazid on **winter cereals** (FOCUS Step 3, single application spray drift scenario). Highest concentration is in bold text

Scenario	Global Max PEC_{SW} (µg / l)	Global Max PEC_{SED} (µg / kg)
D1 (ditch)	**0.316**	1.606
D1 (stream)	0.276	0.178
D2 (ditch)	0.316	1.073
D2 (stream)	0.281	0.948
D3 (ditch)	0.312	0.225
D4 (pond)	0.011	0.119
D4 (stream)	0.247	0.012
D5 (pond)	0.011	0.120
D5 (stream)	0.274	0.019
D6 (ditch)	0.314	0.960
R1 (pond)	0.011	0.229
R1 (stream)	0.205	1.699
R2 (stream)	not performed	not performed
R3 (stream)	0.288	1.039
R4 (stream)	0.205	**1.787**

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
Winter Cereals Single Application D1 – Ditch (surface water) R4 - Stream (Sediment)		0 h	0.316		1.787	
		24 h	0.284	0.299	1.773	1.783
		2 d	0.256	0.284	1.760	1.777
		4 d	0.210	0.258	1.734	1.767
		7 d	0.162	0.226	1.695	1.752
		14 d	0.098	0.176	1.594	1.732
		21d	0.069	0.145	1.504	1.697
		28 d	0.053	0.124	1.424	1.656
		42 d	0.038	0.097	1.270	1.581
		50 d	0.033	0.088	1.183	1.565
		100 d	0.014	0.055	1.508	1.464

Summary of global maximum PEC_{SW} and PEC_{SED} of proquinazid from all drainage (D) and runoff (R) scenarios following the use of proquinazid on **late vines** (FOCUS Step 3, single application spray drift scenario). Highest concentration is in bold text

Scenario	Global Max PEC_{SW} (µg / l)	Global Max PEC_{SED} (µg / kg)

D1 (ditch)	not performed	not performed
D1 (stream)	not performed	not performed
D2 (ditch)	not performed	not performed
D2 (stream)	not performed	not performed
D3 (ditch)	not performed	not performed
D4 (pond)	not performed	not performed
D4 (stream)	not performed	not performed
D5 (pond)	not performed	not performed
D5 (stream)	not performed	not performed
D6 (ditch)	1.268	**3.982**
R1 (pond)	0.048	0.527
R1 (stream)	0.905	1.269
R2 (stream)	1.242	1.242
R3 (stream)	**1.311**	0.370
R4 (stream)	0.930	1.719

21-day Time Weighted Average of proquinazid for each cropping and drainage / runoff scenario in FOCUS Step 3 modelling, following a 90th percentile worst-case, single application. PEC_{SW} in µg / l, PEC_{SED} in µg / kg. Highest concentration is in bold text

21-day Time weighted average, proquinazid				
	Winter cereals		**Vines (late)**	
Scenario	PEC_{SW}	PEC_{SED}	PEC_{SW}	PEC_{SED}
D1 (ditch)	**0.145**	1.588	-	-
D1 (stream)	0.012	0.142	-	-
D2 (ditch)	0.078	0.869	-	-
D2 (stream)	0.067	0.751	-	-
D3 (ditch)	0.015	0.180	-	-
D4 (pond)	0.008	0.119	-	-
D4 (stream)	0.001	0.010	-	-
D5 (pond)	0.008	0.119	-	-
D5 (stream)	0.001	0.015	-	-
D6 (ditch)	0.081	0.865	**0.347**	**3.519**
R1 (pond)	0.008	0.228	0.034	0.526
R1 (stream)	0.003	1.648	0.009	1.211
R2 (stream)	-	-	0.009	1.138
R3 (stream)	0.005	0.974	0.023	0.276
R4 (stream)	0.009	**1.697**	0.009	1.654

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
Vines (Late Appl.) Single Application R3 – Stream (surface water)		0 h	0.316		1.787	
		24 h	0.284	0.299	1.773	1.783
		2 d	0.256	0.284	1.760	1.777
		4 d	0.210	0.258	1.734	1.767
		7 d	0.162	0.226	1.695	1.752

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D6 - Ditch (Sediment)		14 d	0.098	0.176	1.594	1.732
		21d	0.069	0.145	1.504	1.697
		28 d	0.053	0.124	1.424	1.656
		42 d	0.038	0.097	1.270	1.581
		50 d	0.033	0.088	1.183	1.565
		100 d	0.014	0.055	1.508	1.464

STEP 4

21-day Time Weighted Average of proquinazid for each cropping and drainage / runoff scenario in FOCUS Step 4 (single application scenario) modelling. PEC_{SW} in µg / l, PEC_{SED} in µg / kg. Highest concentration is in bold text

21-day Time Weighted Average, proquinazid				
	Winter cereals (3m)		**Vines (late) (16m)**	
Scenario	PEC_{SW}	PEC_{SED}	PEC_{SW}	PEC_{SED}
D1 (ditch)	**0.061**	0.677	-	-
D1 (stream)	0.007	0.081	-	-
D2 (ditch)	0.033	0.372	-	-
D2 (stream)	0.038	0.432	-	-
D3 (ditch)	0.006	0.077	-	-
D4 (pond)	*	*	-	-
D4 (stream)	0.000	0.006	-	-
D5 (pond)	*	*	-	-
D5 (stream)	0.001	0.009	-	-
D6 (ditch)	0.034	0.370	**0.037**	0.389
R1 (pond)	*	*	0.016	0.271
R1 (stream)	0.003	1.647	0.005	1.204
R2 (stream)	-	-	0.003	1.084
R3 (stream)	0.004	0.962	0.003	0.128
R4 (stream)	0.009	**1.693**	0.006	**1.640**

* Pond scenarios were not calculated for cereals because 3m buffer zone provided a more worst case scenario than the default 3.5m distance to the water body incorporated in FOCUS Step 3 modelling.

Summary of global maximum PEC_{SW} and PEC_{SED} of proquinazid from all drainage (D) and runoff (R) scenarios following the use of proquinazid on **winter cereals** (incorporating a 3m buffer zone) (FOCUS Step 4, single application scenario). Highest concentration is in bold text

Scenario	Global Max PEC_{SW} (µg / l)	Global Max PEC_{SED} (µg / kg)
D1 (ditch)	0.134	0.685
D1 (stream)	0.157	0.102
D2 (ditch)	0.134	0.456
D2 (stream)	0.160	0.542
D3 (ditch)	0.132	0.095
D4 (pond)	not calculated*	not calculated*
D4 (stream)	0.141	0.007
D5 (pond)	not calculated*	not calculated*
D5 (stream)	0.156	0.011
D6 (ditch)	0.133	0.409
R1 (pond)	not calculated*	not calculated*
R1 (stream)	0.117	1.698
R2 (stream)	not performed	not performed
R3 (stream)	**0.165**	1.025
R4 (stream)	0.117	**1.783**

* Pond scenarios were not calculated for cereals because 3m buffer zone provided a more worst case scenario than the default 3.5m distance to the water body incorporated in FOCUS Step 3 modelling.

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
Winter Cereals Single Application R3 – Stream (surface water) R4 - Stream (Sediment)		0 h	0.165		1.783	
		24 h	0.000	0.046	1.770	1.779
		2 d	0.000	0.023	1.756	1.774
		4 d	0.000	0.012	1.730	1.764
		7 d	0.000	0.008	1.691	1.748
		14 d	0.000	0.004	1.591	1.729
		21d	0.000	0.004	1.502	1.693
		28 d	0.000	0.003	1.421	1.652
		42 d	0.000	0.002	1.268	1.580
		50 d	0.000	0.002	1.182	1.564
		100 d	0.000	0.002	1.507	1.463

Summary of global maximum PEC_{SW} and PEC_{SED} of proquinazid from all drainage (D) and runoff (R) scenarios following the use of proquinazid on **late vines** (incorporating a 16m buffer zone) (FOCUS Step 4, single application scenario). Highest concentration is in bold text

Scenario	Global Max PEC_{SW} (µg / l)	Global Max PEC_{SED} (µg / kg)
D1 (ditch)	-	-
D1 (stream)	-	-
D2 (ditch)	-	-
D2 (stream)	-	-
D3 (ditch)	-	-
D4 (pond)	-	-
D4 (stream)	-	-
D5 (pond)	-	-
D5 (stream)	-	-
D6 (ditch)	0.137	0.437
R1 (pond)	0.022	0.272
R1 (stream)	0.118	1.269
R2 (stream)	0.161	1.171
R3 (stream)	**0.170**	0.136
R4 (stream)	0.121	**1.705**

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
Vines (Late Appl.) Single Application R3 – Stream (surface water) R4 - Stream (Sediment)		0 h	0.170		1.705	
		24 h	0.001	0.063	1.697	1.701
		2 d	0.000	0.032	1.688	1.697
		4 d	0.000	0.016	1.673	1.690
		7 d	0.000	0.009	1.650	1.678
		14 d	0.000	0.005	1.634	1.654
		21d	0.000	0.003	1.586	1.640
		28 d	0.000	0.002	1.543	1.622
		42 d	0.000	0.002	1.472	1.590
		50 d	0.000	0.001	1.435	1.582
		100 d	0.000	0.001	not calculated *	1.509

* FOCUS TOXSWA reported that the simulated period was too short for the calculation of PEC_{SED}

Metabolite IN-MM671 Parameters used in FOCUSsw step 1 and 2	Molecular weight:246.3 g/ mol Water solubility (mg/L): 0.93 Soil or water metabolite: Soil and water Koc (L/kg): 3297 DT_{50} soil (d): 54 days[†] (Lab geomean value). DT_{50} water/sediment system (d): 300[‡] (default worst case according to aquatic assessment guidelines). DT_{50} water (d): 300[‡] (default worst case according to aquatic assessment guidelines). DT_{50} sediment (d): 300[‡] (default worst case according to aquatic assessment guidelines). Crop interception (%): average crop cover for vines and cereals (50 %) Maximum occurrence observed (% molar basis with respect to the parent) Soil: 65 % AR Water/ Sediment:71 % AR
Parameters used in FOCUSsw step 3 (if performed)	Vapour pressure: not input Koc: 3297 kg/ L 1/n: 1.11 (arithmetic mean) Formation fraction in soil (k_{dp}/k_f): 1.0

Application rate	Crop: Winter cereals, spring cereals, vines (early appl.), vines (late appl.).* Crop interception: 50 % (all crops) Number of applications: 2 (cereals); 4 (vines) Interval (d): 14 days Individual application rate(s): 50 g as/ha (cereals); 75 g as/ ha (vines) Application window: Step 1 & 2: Winter cereals – Northern Europe (March – May) Spring cereals – Northern Europe (March – May) Vines (early appl.) - Northern Europe (June - Sept) Vines (early appl.) - Southern Europe (March – May) Vines (late appl.) - Northern Europe (June - Sept) Vines (late appl.) - Southern Europe (June - Sept) Application window: Step 3: Scenario Winter cereals Vines D1 April 15th – May 31st - D2 April 1st – May 14th - D3 April 1st – May 14th - D4 March 15th – April 30th - D5 March 15th – April 30th - D6 March 1st – April 14th April 1st – June 30th R1 March 15th – April 30th June 1st – Aug 31st R2 - April 15th – July 14th R3 March 1st – April 14th May 1st – July 31st R4 March 1st – April 14th May 1st – July 31st
Main routes of entry	Spray drift and drainflow/ run-off

†For future PECsw assessments the geomean of 81 days should be used for IN-MM671. However the modelling presented was considered to be acceptable.
‡The default FOCUS Kinetics value of 1000 days should be used for future assessments since the whole system value calculated from the water/sediment study, which was considered unacceptable because of too few data points, was 497 days. Therefore 300 days is considered to be potentially not conservative enough. However this amendment is not considered critical to the presented risk assessment since it does not affect initial PEC values.
*Risk assessments for sediment dwelling organisms finish at Step 2. At Step 3, the highest PECsw values are produced from calculations based on single application, but highest PECsed values at Step 3 are obtained from multiple applications. As the Step 3 PECsed values are not required for risk assessment, presentation of PECsw and PECsed are only from single applications. In addition, the highest PEC values for cereals were from winter crops, and for vines from late application. Thus PEC values are only presented for winter cereals and late vines. Note single application PEC values generated by modelling drainflow/runoff for multiple applications, but adding spray drift input appropriate for a single application for only the final application.

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Winter and Spring Cereals	0h	3.09		87.60	
	24h	2.73	2.91	90.04	88.82
	2d	2.72	2.82	89.83	89.38
	4d	2.71	2.77	89.41	89.50
	7d	2.69	2.74	88.80	89.33
	14d	2.65	2.71	87.37	88.71
	21d	2.61	2.68	85.97	88.03
	28d	2.57	2.66	84.59	87.34
	42 d	2.48	2.61	81.90	85.97
	50 d	2.44	2.59	80.40	85.20
	100 d	2.17	2.45	71.63	80.56

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Vines (late appl.)	0h	11.74		262.81	
	24h	8.65	10.20	285.20	274.01
	2d	8.63	9.42	284.54	279.44
	4d	8.59	9.01	283.23	281.66
	7d	8.53	8.82	281.27	281.91
	14d	8.39	8.64	276.76	280.46
	21d	8.26	8.54	272.32	278.49
	28d	8.13	8.45	267.95	276.40
	42 d	7.87	8.30	259.42	272.15
	50 d	7.72	8.22	254.67	269.74
	100 d	6.88	7.76	226.89	255.12

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Winter and Spring Cereals Multiple Applications Northern EU	0 h	0.33		9.89	
	24 h	0.30	0.31	9.87	9.88
	2 d	0.30	0.31	9.84	9.87
	4 d	0.30	0.30	9.80	9.84
	7 d	0.30	0.30	9.73	9.81
	14 d	0.29	0.30	9.57	9.73
	21 d	0.29	0.29	9.42	9.65
	28 d	0.28	0.29	9.27	9.58
	42 d	0.27	0.29	8.97	9.42
	50 d	0.27	0.28	8.81	9.34
	100 d	0.24	0.27	7.85	8.83
Vines (late appl.) Multiple Applications Southern EU	0 h	1.64		47.05	
	24 h	1.43	1.53	46.94	47.00
	2 d	1.42	1.48	46.83	46.94
	4 d	1.42	1.45	46.62	46.83
	7 d	1.41	1.43	46.30	46.67
	14 d	1.38	1.41	45.55	46.30
	21 d	1.36	1.40	44.82	45.93
	28 d	1.34	1.39	44.10	45.56
	42 d	1.30	1.37	42.70	44.84
	50 d	1.27	1.35	41.92	44.44
	100 d	1.14	1.28	37.34	42.01

Metabolite IN-MM986	Molecular weight: 330.1 g/ mol
Parameters used in FOCUSsw step 1 and 2	Water solubility (mg/L): 0.73 Soil or water metabolite: Soil Koc (L/kg): 2376 DT_{50} soil (d): 16 days (Lab geomean value). DT_{50} water/sediment system (d): 300 (default worst case according to aquatic assessment guidelines). DT_{50} water (d): 300 (default worst case according to aquatic assessment guidelines). DT_{50} sediment (d): 300 (default worst case according to aquatic assessment guidelines). Crop interception (%): average crop cover for vines and cereals (50 %) Maximum occurrence observed (% molar basis with respect to the parent) Soil: 32.8 % AR Water/ Sediment:0.2 % AR
Application rate	Crop: Winter cereals, spring cereals, vines (early appl.), vines (late appl.). Crop interception: 50 % (all crops) Number of applications: 2 (cereals); 4 (vines) Interval (d): 14 days Individual application rate(s): 50 g as/ha (cereals); 75 g as/ ha (vines) Application window: Step 1 & 2: Winter cereals – Northern Europe (March – May) Spring cereals – Northern Europe (March – May) Vines (early appl.) - Northern Europe (June - Sept) Vines (early appl.) - Southern Europe (March – May) Vines (late appl.) - Northern Europe (June - Sept) Vines (late appl.) - Southern Europe (June - Sept)
Main routes of entry	Drainflow/ run-off

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Winter and Spring Cereals	0h	2.33		55.26	
	24h	2.32	2.32	55.16	55.22
	2d	2.32	2.32	55.03	55.16
	4d	2.31	2.32	54.78	55.03
	7d	2.29	2.31	54.40	54.84
	14d	2.25	2.29	53.53	54.40
	21d	2.22	2.27	52.67	53.97
	28d	2.18	2.25	51.82	53.54
	42 d	2.11	2.22	50.17	52.69
	50 d	2.07	2.07	49.25	52.21
	100 d	1.85	1.85	43.88	49.36

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Vines (late appl.)	0h	6.99		165.83	
	24h	6.97	6.98	165.53	165.68
	2d	6.95	6.97	165.15	165.51
	4d	6.92	6.95	164.38	165.14
	7d	6.87	6.93	163.25	164.57
	14d	6.76	6.87	160.63	163.25
	21d	6.65	6.82	158.05	161.95
	28d	6.55	6.76	155.52	160.66
	42 d	6.34	6.65	150.57	158.11
	50 d	6.22	6.59	147.81	156.69
	100 d	5.54	6.23	131.68	148.14

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Winter and Spring Cereals Multiple Applications Northern EU	0 h	0.15		3.51	
	24 h	0.15	0.15	3.50	3.50
	2 d	0.15	0.15	3.49	3.50
	4 d	0.15	0.15	3.48	3.49
	7 d	0.15	0.15	3.45	3.48
	14 d	0.14	0.15	3.40	3.45
	21 d	0.14	0.14	3.34	3.42
	28 d	0.14	0.14	3.29	3.40
	42 d	0.13	0.14	3.18	3.34
	50 d	0.13	0.14	3.13	3.31
	100 d	0.12	0.13	2.78	3.13
Vines (late appl.) Multiple Applications Southern EU	0 h	0.56		13.40	
	24 h	0.56	0.56	13.37	13.39
	2 d	0.56	0.56	13.34	13.37
	4 d	0.56	0.56	13.28	13.34
	7 d	0.56	0.56	13.19	13.30
	14 d	0.55	0.56	12.98	13.19
	21 d	0.54	0.55	12.77	13.08
	28 d	0.53	0.55	12.56	12.98
	42 d	0.51	0.54	12.17	12.77
	50 d	0.50	0.53	11.94	12.66
	100 d	0.45	0.50	10.64	11.97

Metabolite IN-MM991	Molecular weight: 204.2 g/ mol
Parameters used in FOCUSsw step 1 and 2	Water solubility (mg/L): 0.73 Soil or water metabolite: Soil Koc (L/kg): 264 DT_{50} soil (d): 27 days (Lab geomean value)†. DT_{50} water/sediment system (d): 300 (default worst case according to aquatic assessment guidelines). DT_{50} water (d): 300 (default worst case according to aquatic assessment guidelines). DT_{50} sediment (d): 300 (default worst case according to aquatic assessment guidelines). Crop interception (%): average crop cover for vines and cereals (50 %) Maximum occurrence observed (% molar basis with respect to the parent) Soil: 13.4 % AR Water/ Sediment:1.2 % AR
Application rate	Crop: Winter cereals, spring cereals, vines (early appl.), vines (late appl.). Crop interception: 50 % (all crops) Number of applications: 2 (cereals); 4 (vines) Interval (d): 14 days Individual application rate(s): 50 g as/ha (cereals); 75 g as/ ha (vines) Application window: Step 1 & 2: Winter cereals – Northern Europe (March – May) Spring cereals – Northern Europe (March – May) Vines (early appl.) - Northern Europe (June - Sept) Vines (early appl.) - Southern Europe (March – May) Vines (late appl.) - Northern Europe (June - Sept) Vines (late appl.) - Southern Europe (June - Sept)
Main routes of entry	Drainflow/ run-off

† The Keyport loam was not considered to provide an appropriate fit to inform an input parameter for FOCUS modelling. Therefore the longest DT50 value of 22 days should be used in future modelling. This input value used in the presented modelling is more worse-case than that which should be used. It is also not considered that this change will affect PEC values significantly for the presented modelling and therefore the presented PECs are considered acceptable.

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Winter and Spring Cereals	0h	1.82		4.79	
	24h	1.81	1.82	4.79	4.79
	2d	1.81	1.81	4.77	4.78
	4d	1.80	1.81	4.75	4.77
	7d	1.79	1.80	4.72	4.76
	14d	1.76	1.79	4.64	4.72
	21d	1.73	1.77	4.57	4.68
	28d	1.70	1.76	4.50	4.64
	42 d	1.65	1.73	4.35	4.57
	50 d	1.62	1.72	4.27	4.53
	100 d	1.44	1.62	3.81	4.28

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Vines (late appl.)	0h	5.49		14.36	
	24h	5.46	5.48	14.43	14.39
	2d	5.45	5.47	14.39	14.40
	4d	5.43	5.45	14.33	14.38
	7d	5.39	5.43	14.23	14.33
	14d	5.30	5.39	14.00	14.22
	21d	5.22	5.35	13.77	14.11
	28d	5.13	5.30	13.55	14.00
	42 d	4.97	5.22	13.12	13.78
	50 d	4.88	5.17	12.88	13.65
	100 d	4.35	4.89	11.48	12.91

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Winter and Spring Cereals Multiple Applications Northern EU	0 h	0.14		0.38	
	24 h	0.14	0.14	0.38	0.38
	2 d	0.14	0.14	0.37	0.38
	4 d	0.14	0.14	0.37	0.37
	7 d	0.14	0.14	0.37	0.37
	14 d	0.14	0.14	0.36	0.37
	21 d	0.14	0.14	0.36	0.37
	28 d	0.13	0.14	0.35	0.36
	42 d	0.13	0.14	0.34	0.36
	50 d	0.13	0.13	0.33	0.36
	100 d	0.11	0.13	0.30	0.34
Vines (late appl.) Multiple Applications Southern EU	0 h	0.63		1.66	
	24 h	0.63	0.63	1.66	1.66
	2 d	0.63	0.63	1.65	1.66
	4 d	0.63	0.63	1.65	1.65
	7 d	0.62	0.63	1.64	1.65
	14 d	0.61	0.62	1.61	1.64
	21 d	0.60	0.62	1.58	1.62
	28 d	0.59	0.61	1.56	1.61
	42 d	0.57	0.60	1.51	1.58
	50 d	0.56	0.60	1.48	1.57
	100 d	0.50	0.56	1.32	1.48

Metabolite IN-MT884 Parameters used in FOCUSsw step 1 and 2	Molecular weight: 312.3 g/ mol Water solubility (mg/L): 0.73 Soil or water metabolite: water (aqueous photolysis) Koc (L/kg): 10 DT_{50} soil (d): 300 (default worst case according to aquatic assessment guidelines). DT_{50} water/sediment system (d): 300 (default worst case according to aquatic assessment guidelines). DT_{50} water (d): 300 (default worst case according to aquatic assessment guidelines). DT_{50} sediment (d): 300 (default worst case according to aquatic assessment guidelines). Crop interception (%): average crop cover for vines and cereals (50 %) Maximum occurrence observed (% molar basis with respect to the parent) Soil: 0 % AR Water/ Sediment:30.5 % AR
Application rate	Crop: Winter cereals, spring cereals, vines (early appl.), vines (late appl.). Crop interception: 50 % (all crops) Number of applications: 2 (cereals); 4 (vines) Interval (d): 14 days Individual application rate(s): 50 g as/ha (cereals); 75 g as/ ha (vines) Application window: Step 1 & 2: Winter cereals – Northern Europe (March – May) Spring cereals – Northern Europe (March – May) Vines (early appl.) - Northern Europe (June - Sept) Vines (early appl.) - Southern Europe (March – May) Vines (late appl.) - Northern Europe (June - Sept) Vines (late appl.) - Southern Europe (June - Sept)
Main routes of entry	Spray drift

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Winter and Spring Cereals	0h	0.24		0.00	
	24h	0.23	0.23	1.64	0.82
	2d	0.23	0.23	1.63	1.23
	4d	0.23	0.23	1.63	1.43
	7d	0.23	0.23	1.62	1.51
	14d	0.22	0.23	1.59	1.56
	21d	0.22	0.23	1.56	1.56
	28d	0.22	0.23	1.54	1.56
	42 d	0.21	0.22	1.49	1.55
	50 d	0.21	0.22	1.46	1.53
	100 d	0.18	0.21	1.30	1.46

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Vines (late appl.)	0h	2.05		0.00	
	24h	2.02	2.04	14.30	7.15
	2d	2.02	2.03	14.27	10.72
	4d	2.01	2.02	14.20	12.48
	7d	1.99	2.01	14.10	13.19
	14d	1.96	2.00	13.88	13.59
	21d	1.93	1.98	13.65	13.65
	28d	1.90	1.97	13.44	13.62
	42 d	1.84	1.93	13.01	13.49
	50 d	1.81	1.92	12.77	13.39
	100 d	1.61	1.81	11.38	12.73

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Winter and Spring Cereals Multiple Applications Northern EU	0 h	0.20		1.36	
	24 h	0.20	0.20	1.36	1.36
	2 d	0.20	0.20	1.36	1.36
	4 d	0.20	0.20	1.35	1.36
	7 d	0.20	0.20	1.34	1.35
	14 d	0.20	0.20	1.32	1.34
	21 d	0.19	0.20	1.30	1.33
	28 d	0.19	0.20	1.28	1.32
	42 d	0.18	0.19	1.24	1.30
	50 d	0.18	0.19	1.22	1.29
	100 d	0.16	0.18	1.08	1.22
Vines (late appl.) Multiple Applications Southern EU	0 h	1.61		10.78	
	24 h	1.60	1.60	10.77	10.78
	2 d	1.60	1.60	10.75	10.77
	4 d	1.59	1.60	10.71	10.75
	7 d	1.57	1.59	10.63	10.71
	14 d	1.55	1.57	10.46	10.63
	21 d	1.52	1.56	10.29	10.55
	28 d	1.50	1.55	10.13	10.46
	42 d	1.45	1.52	9.81	10.30
	50 d	1.42	1.51	9.63	10.20
	100 d	1.27	1.43	8.58	9.65

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: FOCUS PELMO 3.3.2 Scenarios (list of names):Chateaudun, Hamburg, Jokioinen (cereals only), Kremsmunster, Okehampton (cereals only), Piacenza (winter cereals and vines only), Porto, Sevilla (winter cereals and vines only), Thiva (winter cereals and vines only). Crop: Winter cereals, spring cereals, grapevines Parent: Geometric mean parent DT_{50lab} 60 d (normalised to 10kPa or pF2, 20 °C with Q10 of 2.2). K_{OC} parent: 12870 mL/ g, $^1/_n$= 0.94 (arithmetic mean). Metabolites: IN-MM671: Geometric mean parent DT_{50lab} 54 d† (normalised to 10kPa or pF2, 20 °C with Q10 of 2.2). K_{OC} parent: 3297 mL/ g, $^1/_n$= 1.11 (arithmetic mean) Formation Fraction: See below metabolism scheme Metabolites: IN-MM986: Geometric mean parent DT_{50lab} 15 d (normalised to 10kPa or pF2, 20 °C with Q10 of 2.2). K_{OC} parent: 2376 mL/ g, $^1/_n$= 0.94 (arithmetic mean). Formation Fraction: See below metabolism scheme Metabolites: IN-MM991: Geometric mean parent DT_{50lab} 27 d†† (normalised to 10kPa or pF2, 20 °C with Q10 of 2.2). K_{OC} parent: 264 mL/ g, $^1/_n$= 0.82 (arithmetic mean). Formation Fraction: See below metabolism scheme
Application rate	Application rate: Cereals: 50 g as/ ha. Vines: 75 g as/ ha No. of applications: Cereals: 2 Vines:4 Crop Interception: Cereals: 50 – 70 % Vines: 60 – 85 % Time of application (month or season): See below Table

†For future PECgroundwater assessments the geomean of 81 days should be used for IN-MM671. However the modelling presented was considered to be acceptable in view of the high Kfoc value of 2333 L/ kg used.
†† The Keyport loam was not considered to provide an appropriate fit to inform an input parameter for FOCUS modelling. Therefore the longest DT50 value of 22 days should be used in future modelling. This input value used in the presented modelling is more worse-case than that which should be used. It is also not considered that this change will affect PEC values significantly for the presented modelling.

Metabolism Scheme

Metabolism — Proquinazid may follow two degradation pathways: Pathway 1 (or A) – 100% formation of IN-MM671, which then degrades further with 100% formation of IN-MM991. Pathway 2 (or B) - proquinazid degrades to both IN-MM671 (26%) and IN-MM986 (74%). 100% of the formed IN-MM671 then degrades to IN-MM991. In both pathways, IN-MM991 and IN-MM986 degrade to CO_2 and bound residues.

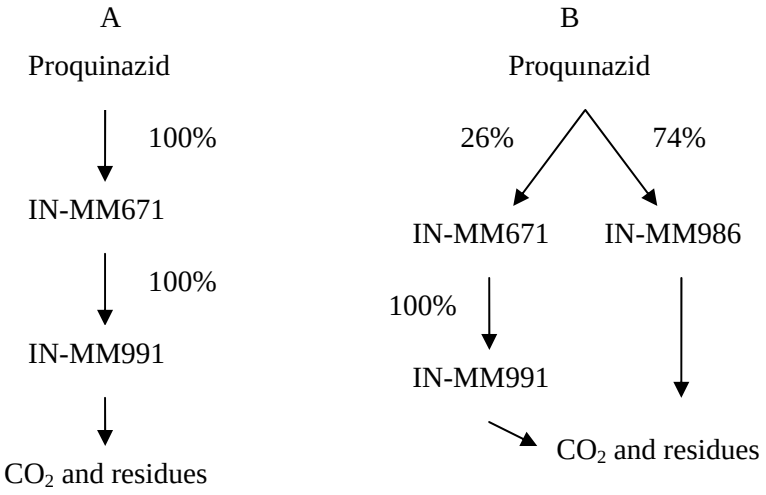


Table of Application Dates

Crop	*Location*	*Application dates*			
		1	*2*	*3*	*4*
Winter cereals	*Châteaudun*	*15/03*	*01/04*	-	-
	Hamburg	*01/04*	*15/04*	-	-
	Jokioinen	*15/04*	*01/05*	-	-
	Kremsmünster	*15/03*	*01/04*	-	-
	Okehampton	*01/04*	*15/04*	-	-
	Piacenza	*01/03*	*15/03*	-	-
	Porto	*15/02*	*01/03*	-	-
	Sevilla	*15/02*	*01/03*	-	-
	Thiva	*01/02*	*15/02*	-	-
Spring cereals	*Châteaudun*	*15/04*	*01/05*	-	-
	Hamburg	*01/05*	*15/05*	-	-
	Jokioinen	*15/05*	*01/06*	-	-
	Kremsmünster	*15/04*	*01/05*	-	-
	Okehampton	*01/05*	*15/05*	-	-
	Porto	*15/03*	*01/04*	-	-
Grape vines	*Châteaudun*	*15/06*	*01/07*	*15/07*	*01/08*
	Hamburg	*15/06*	*01/07*	*15/07*	*01/08*
	Kremsmünster	*15/06*	*01/07*	*15/07*	*01/08*
	Piacenza	*15/05*	*01/06*	*15/06*	*01/07*
	Porto	*15/04*	*01/05*	*15/05*	*01/06*
	Sevilla	*01/04*	*15/04*	*01/05*	*15/05*
	Thiva	*15/04*	*01/05*	*15/05*	*01/06*

PEC(gw) - FOCUS modelling results for application to winter cereals - Pathway 1(or A), values are 80th percentile annual average concentration at 1m

Model /Crop	Scenario	Proquinazid (µg/L)	Metabolite (µg/L)		
			IN-MM 671	IN-MM 986	IN-MM 991
	Chateaudun	< 0.001	< 0.001	< 0.001	< 0.001
	Hamburg	< 0.001	< 0.001	< 0.001	< 0.001
	Jokioinen	< 0.001	< 0.001	< 0.001	< 0.001
	Kremsmunster	< 0.001	< 0.001	< 0.001	< 0.001
	Okehampton	< 0.001	< 0.001	< 0.001	< 0.001
	Piacenza	< 0.001	< 0.001	< 0.001	< 0.001
	Porto	< 0.001	< 0.001	< 0.001	< 0.001
	Sevilla	< 0.001	< 0.001	< 0.001	< 0.001
	Thiva	< 0.001	< 0.001	< 0.001	< 0.001

PEC(gw) - FOCUS modelling results for application to winter cereals - Pathway 2(or B), values are 80th percentile annual average concentration at 1m

Model /Crop	Scenario	Proquinazid (µg/L)	Metabolite (µg/L)	
			IN-MM 671	IN-MM 991
	Chateaudun	< 0.001	< 0.001	< 0.001
	Hamburg	< 0.001	< 0.001	< 0.001
	Jokioinen	< 0.001	< 0.001	< 0.001
	Kremsmunster	< 0.001	< 0.001	< 0.001
	Okehampton	< 0.001	< 0.001	< 0.001
	Piacenza	< 0.001	< 0.001	< 0.001
	Porto	< 0.001	< 0.001	< 0.001
	Sevilla	< 0.001	< 0.001	< 0.001
	Thiva	< 0.001	< 0.001	< 0.001

PEC(gw) - FOCUS modelling results for application to spring cereals - Pathway 1(or A), values are 80th percentile annual average concentration at 1m

Model /Crop	Scenario	Proquinazid (µg/L)	Metabolite (µg/L)		
			IN-MM 671	IN-MM 986	IN-MM 991
	Chateaudun	< 0.001	< 0.001	< 0.001	< 0.001
	Hamburg	< 0.001	< 0.001	< 0.001	< 0.001
	Jokioinen	< 0.001	< 0.001	< 0.001	< 0.001
	Kremsmunster	< 0.001	< 0.001	< 0.001	< 0.001
	Okehampton	< 0.001	< 0.001	< 0.001	< 0.001
	Piacenza	-	-	-	-
	Porto	< 0.001	< 0.001	< 0.001	< 0.001
	Sevilla	-	-	-	-
	Thiva	-	-	-	-

PEC(gw) - FOCUS modelling results for application to spring cereals - Pathway 2(or B), values are 80th percentile annual average concentration at 1m

Model /Crop	Scenario	Proquinazid (µg/L)	Metabolite (µg/L)	
			IN-MM 671	IN-MM 991
	Chateaudun	< 0.001	< 0.001	< 0.001
	Hamburg	< 0.001	< 0.001	< 0.001
	Jokioinen	< 0.001	< 0.001	< 0.001
	Kremsmunster	< 0.001	< 0.001	< 0.001
	Okehampton	< 0.001	< 0.001	< 0.001
	Piacenza	-	-	-
	Porto	< 0.001	< 0.001	< 0.001
	Sevilla	-	-	-
	Thiva	-	-	-

PEC(gw) - FOCUS modelling results for application to grape vines - Pathway 1(or A), values are 80th percentile annual average concentration at 1m

Model /Crop	Scenario	Proquinazid (µg/L)	Metabolite (µg/L)		
			IN-MM 671	IN-MM 986	IN-MM 991
	Chateaudun	< 0.001	< 0.001	< 0.001	< 0.001
	Hamburg	< 0.001	< 0.001	< 0.001	< 0.001
	Jokioinen	-	-	-	-
	Kremsmunster	< 0.001	< 0.001	< 0.001	< 0.001
	Okehampton	-	-	-	-
	Piacenza	< 0.001	< 0.001	< 0.001	< 0.001
	Porto	< 0.001	< 0.001	< 0.001	< 0.001
	Sevilla	< 0.001	< 0.001	< 0.001	< 0.001
	Thiva	< 0.001	< 0.001	< 0.001	< 0.001

PEC(gw) - FOCUS modelling results for application to grape vines - Pathway 2(or B), values are 80th percentile annual average concentration at 1m

Model /Crop	Scenario	Proquinazid (µg/L)	Metabolite (µg/L)	
			IN-MM 671	IN-MM 991
	Chateaudun	< 0.001	< 0.001	< 0.001
	Hamburg	< 0.001	< 0.001	< 0.001
	Jokioinen	-	-	-
	Kremsmunster	< 0.001	< 0.001	< 0.001
	Okehampton	-	-	-
	Piacenza	< 0.001	< 0.001	< 0.001
	Porto	< 0.001	< 0.001	< 0.001
	Sevilla	< 0.001	< 0.001	< 0.001
	Thiva	< 0.001	< 0.001	< 0.001

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

Direct photolysis in air ‡	No data submitted, not required
Quantum yield of direct phototransformation	0.00745
Photochemical oxidative degradation in air ‡	Half life of 4 hours calculated by the method of Atkinson, assuming concentration of 1.5 x 10^6 OH radicals per cm^3 and irradiation based on a 12 hour day
Volatilisation ‡	from plant surfaces: approx. 14% AR after 24 hours
	from soil: approx. 0.38% AR after 24 hours
Metabolites	None

PEC (air)

Method of calculation	No guidance on calculation.

$PEC_{(a)}$

Maximum concentration	Expected to be negligible.

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: Proquinazid, metabolites IN-MM671, IN-MM986, IN-MM991 Surface water: Proquinazid, metabolites IN-MM671, IN-MM986, IN-MM991, IN-MM884 Sediment: Proquinazid, metabolites IN-MM671, IN-MM986, IN-MM991, IN-MM884 Groundwater: Proquinazid, metabolites IN-MM671, IN-MM986, IN-MM991 Air: Proquinazid

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

Soil (indicate location and type of study)	Not applicable, new active substance
Surface water (indicate location and type of study)	Not applicable, new active substance
Ground water (indicate location and type of study)	Not applicable, new active substance
Air (indicate location and type of study)	Not applicable, new active substance

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Candidate R53

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Colinus virginianus	a.s.	Acute	LC50 >2250	
Colinus virginianus	Preparation	Acute	LC50 >2250 product	
Colinus virginianus	a.s.	Short-term	LC50 1371	5620
Anas platyrhynchos	a.s.	Short-term	LC50 3110	5620
Colinus virginianus	a.s.	Long-term	NOEC 7.78	85
Anas platyrhynchos	a.s.	Long-term	29.6 female 31.5 male	255 255
Mammals ‡				
Rat	a.s.	Acute	4846	
Rat	Preparation	Acute	>2000 product*	
Rat	IN-MM671	Acute	2052	
Rat	a.s.	Long-term	35.1	>600
Additional higher tier studies ‡				

*Proquinazid 200 g/l EC

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

Cereals total dose 0.1kg a.s./ha 2 x foliar applications

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Large herbivorous birds (300g)	Acute		>574	10
Small insectivorous bird (10g)	Acute		>832	10
Large herbivorous birds (300g)	Short-term		>594	10
Small insectivorous bird (10g)	Short-term		>909	10
Large herbivorous birds (300g)	Long-term		6.38	5
Small insectivorous bird (10g)	Long-term		5.16	5
Earthworm-eating small bird	Long-term		10.6*	5
Fish-eating bird	Long-term		16.3**	5
Tier 1 (Mammals) Propaquinazid				
Small herbivorous mammal (25g)	Acute		393***	10
Insectivorous mammal (10g)	Acute		8791***	10
Small herbivorous mammal (25g)	Long-term		9.06***	5
Insectivorous mammal (10g)	Long-term		218***	5
Earthworm-eating mammal	Long-term		37.6*	5
Fish-eating mammal	Long-term		119**	5
Tier 1 Mammals (formulation)				
Small herbivorous mammal (25g)	Acute		16.2****	10
Insectivorous mammal (10g)	Acute		454****	10
Tier 1 Mammals (IN-MM671)				
Small herbivorous mammal (25g)	Acute		166	10
Insectivorous mammal (10g)	Acute		4653	10

*Exposure estimate based on a 21 day TWA soil (earthworm) or water PEC (fish) from 2 applications each of 50 g a.s./ha with 50% crop interception and a 14 day spray interval
**Exposure estimate based on an initial Step 1 PECsw (0.00276 mg/l) from 2 applications each of 50 g a.s./ha with a 14 day spray interval
***Amended from Volume 3 values due to correction of acute or long-term RUD values (as per SANCO guidance)
****Amended from Volume 3 values due to correction of mammalian (rat) formulation LD50 to >200 mg a.s./kg/bw (equivalent to >2000 mg formulation/kg bw)

TER values for uses in vines at different GAP application rates (0.2 – 0.3 kg a.s./ha)

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Vines total dose 0.3kg a.s./ha 4 x foliar applications (early/late)				
Small insectivorous bird (10g)	Acute		>555	10
Small insectivorous bird (10g)	Short-term		>606	10
Small insectivorous bird (10g)	Long-term		**3.44**	5
Earthworm-eating small bird	Long-term		**4.02***	5
Fish-eating bird	Long-term		81.6*	5
Vines total dose 0.2kg a.s./ha 4 x foliar applications (early/late)				
Small insectivorous bird (10g)	Long-term		5.16	5
Earthworm-eating small bird	Long-term		6.01**	5
Higher tier refinement (Birds)				
Vines total dose 0.3kg a.s./ha 4 x foliar applications (early/late)				
Small insectivorous bird (10g) with refined RUD value of 17.05	Long-term		5.85	5
Tier 1 (Mammals) proquinazid use at dose 0.3kg a.s./ha 4 x foliar applications (early/late)				
Small herbivorous mammal (25g)	Acute		402***	10
Small herbivorous mammal (25g)	Long-term		8.72***	5
Earthworm-eating mammal	Long-term		17.9**	5
Fish-eating mammal	Long-term		24.3#	5

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Mammals) formulationuse at dose 0.3kg a.s./ha 4 x foliar applications (early/late)				
Small herbivorous mammal (25g)	Acute		16.6****	10
Tier 1 (Mammals) IN-MM671use at dose 0.3kg a.s./ha 4 x foliar applications (early/late)				
Small herbivorous mammal (25g)	Long-term		170*****	5

Exposure estimate based on an initial Step 1 PECsw (0.01357 mg/l) from 4 applications each of 75 g a.s./ha with a 14 day spray interval
*Exposure estimate based on a 21 day TWA soil (earthworm) or 21 day FOCUS Step 3 water PEC (fish) from 4 applications each of 75 g a.s./ha with 50% crop interception and a 14 day spray interval
**Exposure estimate based on a 21 day TWA soil PEC from 4 applications each of 50 or 75 g a.s./ha with 50% crop interception and 14 day spray interval
***Amended from Volume 3 values due to correction of acute or long-term RUD values (as per SANCO guidance)
****Slightly amended from Volume 3 due to use of a corrected MAF of 1.36 (instead of 1.38) and amended from Volume 3 values due to correction of mammalian (rat) formulation LD50 to >200 mg a.s./kg bw (equivalent to >2000 mg formulation/kg bw)
*****Slightly amended from Volume 3 due to use of a corrected MAF of 1.36 (instead of 1.38)

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss	a.s.	96 hr	Mortality, EC_{50}	0.349 mg a.s./l
Lepomis macrochirus	a.s.	96 hr	Mortality, EC_{50}	0.454 mg a.s./l
Cyprinodon variegates	a.s.	96 hr	Mortality, EC_{50}	>0.58 mg a.s./l
Oncorhynchus mykiss	a.s.	90 d	NOEC	0.0030 mg a.s./l
Cyprinodon variegates	a.s.	36 d	NOEC	0.00872 mg a.s./l
Oncorhynchus mykiss	Preparation	96 hr	Mortality, EC_{50}	2.3 mg product/l (0.446 mg a.s./l)
Oncorhynchus mykiss	IN-MM671	96 hr	Mortality, EC_{50}	2.2 mg metabolite/l
Lepomis macrochirus	IN-MM671	96 hr	Mortality, EC_{50}	4.2 mg metabolite/l
Oncorhynchus mykiss	IN-MM986	96 hr	Mortality, EC_{50}	>1.03 mg metabolite/l
Oncorhynchus mykiss	IN-MM991	96 hr	Mortality, EC_{50}	28.4 mg metabolite/l
Aquatic invertebrate				
Daphnia magna	a.s.	48 h	Mortality, EC_{50}	0.287 mg a.s./l
Crassostrea virginica	a.s.	96 hr	Mortality, EC_{50}	0.219 mg a.s./l
Mysidopsis bahia	a.s.	96 hr	Mortality, EC_{50}	0.11 mg a.s./l
Daphnia magna	a.s.	21 d	Reproduction, NOEC	0.0018 mg a.s/l
Mysidopsis bahia	a.s.	28 d	Reproduction, NOEC	0.0105 mg a.s./l
Daphnia magna	Preparation	48 hr	Mortality, EC_{50}	1.8 mg product/l (0.349 mg a.s./l)
Daphnia magna	IN-MM671	48 hr	Mortality, EC_{50}	5.4 mg metabolite/l
Daphnia magna	IN-MM986	48 hr	Mortality, EC_{50}	>0.791 mg metabolite/l
Daphnia magna	IN-MM991	48 hr	Mortality, EC_{50}	>45.5 mg metabolite/l

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Daphnia magna	IN-MT884	48 hr	Mortality, EC_{50}	>114.0 mg metabolite/l
Daphnia magna	IN-MM671	21 day	NOEC	0.519 mg metabolite/l
Sediment dwelling organisms				
Chironomus riparius	a.s.	28 d	NOEC	0.456 mg a.s./l
Algae				
Anabaena flos-aquae	a.s.	72 h	Biomass: E_bC_{50}	>0.884 mg a.s./l
Pseudokirchneriella subcapitata	a.s.	72 h	Biomass: E_bC_{50}	0.684 mg a.s./l
Navicula pelliculosa	*a.s.*	*72 h*	*Biomass: E_bC_{50}*	*0.25 mg a.s./l*
Pseudokirchneriella subcapitata	*Preparation*	*72 h*	*Biomass: E_bC_{50}*	*1.3 mg product/l (0.259 mg a.s./l)*
Pseudokirchneriella subcapitata	*IN-MM671*	*72 h*	*Biomass: E_bC_{50}*	*0.725 mg metabolite/l*
Pseudokirchneriella subcapitata	*IN-MM986*	*72 h*	*Biomass: E_bC_{50}*	*0.96 mg metabolite/l*
Pseudokirchneriella subcapitata	*IN-MM991*	*72 h*	*Biomass: E_bC_{50}*	*1.1 mg metabolite/l*
Higher plant				
Lemna gibba	a.s.	14 d	Fronds, EC_{50}	>0.2 mg a.s./l
Microcosm or mesocosm tests				
Indicate if not required				

[1] indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether end points are presented as units of preparation or a.s.

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

FOCUS Step1

Cereals total dose 0.1kg a.s./ha 2 x foliar applications

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	Annex VI Trigger[1]

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	Annex VI Trigger[1]
a.s.	Fish (*O. mykiss*)	0.349	Acute			126.4	100
a.s.	Fish (*O. mykiss*)	0.0030	Chronic			**1.09**	10
a.s.	Aquatic invertebrates (*D. magna*)	0.287	Acute			104.0	100
a.s.	Aquatic invertebrates (*M. bahia*)	0.0105	Acute			**39.9**	100
a.s.	Aquatic invertebrates (*D. magna*)	0.0018	Chronic			**0.65**	10
a.s.	Algae (*N. pelliculosa*)	0.25	Chronic			90.6	10
a.s.	Algae (*P. subcapitata*)	>0.12	Chronic			>43.5	10
a.s.	Higher plants[2] (L. gibba)	0.2	Chronic			72.5	10
a.s.	Sediment-dwelling[3] organisms (*C. riparius*)	0.456	Chronic			13.36	10
IN-MM671	Fish (*O. mykiss*)	2.2	Acute			712.0	100
IN-MM671	Aquatic invertebrates (*D. magna*)	5.4	Acute			1747.6	100
IN-MM671	Algae (*P. subcapitata*)	0.725	Chronic			234.6	10
IN-MM671	Aquatic invertebrates (*D. magna*)	0.519	Chronic			168.0	10
IN-MM986	Fish (*O. mykiss*)	>1.03	Acute			>442.1	100
IN-MM986	Aquatic invertebrates(*D. magna*)	>0.791	Acute			>3394.9	100
IN-MM986	Algae (*P. subcapitata*)	0.96	Chronic			412.0	10
IN-MM991	Fish (*O. mykiss*)	28.4	Acute			15604	100
IN-MM991	Aquatic invertebrates (*P. subcapitata*)	>45.5	Acute			>25000	100

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	Annex VI Trigger[1]
IN-MM991	Algae (*P. subcapitata*)	1.1	Chronic			604.4	10
IN-MT884	Aquatic invertebrates (*D. magna*)	>114.0	Acute			>47500	100

[1]If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[2] only required for herbicides
[3]consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used

Vines total dose 0.3kg a.s./ha 4 x foliar applications

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	Annex VI Trigger[1]
a.s.	Fish *(O. mykiss)*	0.349	Acute			**25.8**	100
a.s.	Fish *(O. mykiss)*	0.0030	Chronic			**0.22**	10
a.s.	Aquatic invertebrates *(D magna)*	0.287	Acute			**21.2**	100
a.s.	Aquatic invertebrates *(M. bahia)*	0.11	Acute			**8.1**	100
a.s.	Aquatic invertebrates *(D magna)*	0.0018	Chronic			**0.13**	10
a.s.	Algae (*N. pelliculosa*)	0.25	Chronic			18.5	10
a.s.	Algae (*P. subcapitata*)	0.259	Chronic			19.1	10
a.s.	Higher plants[2] (*L. gibba*)	0.2	Chronic			14.8	10
a.s.	Sediment-dwelling[3] organisms (*C. riparius*)	0.456	Chronic			4.24	10
IN-MM671	Fish (*O. mykiss*)	2.2	Acute			187.4	100
IN-MM671	Aquatic invertebrates (*D. magna*)	5.4	Acute			460.0	100

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	Annex VI Trigger[1]
IN-MM671	Algae (*P. subcapitata*)	0.725	Chronic			61.75	10
IN-MM671	Aquatic invertebrates (*D. magna*)	0.519	Chronic			44.21	10
IN-MM986	Fish (*O. mykiss)*	>1.03	Acute			147.4	100
IN-MM986	Aquatic invertebrates (*D. magna*)	>0.791	Acute			1131.6	100
IN-MM986	Algae (*P. subcapitata*)	0.96	Chronic			137.3	10
IN-MM991	Fish (*O. mykiss)*	28.4	Acute			5173.0	100
IN-MM991	Aquatic invertebrates (*D. magna*)	>45.5	Acute			8287.8	100
IN-MM991	Algae (*P. subcapitata*)	1.1	Chronic			200.4	10
IN-MT884	Aquatic invertebrates (*D. magna*)	>114.0	Acute			55610	100

FOCUS Step 2

Cereals total dose 0.1kg a.s./ha 2 x foliar applications

Test substance	N/S[1]	Organism[2]	Toxicity end point (mg/L)	Time scale	PEC[3]	TER	Annex VI Trigger[4]
a.s.		Aquatic invertebrates (*M. bahia*)	0.11	Acute		239.1	100
a.s.		Fish (*O. mykiss*)	0.349	Chronic		**6.52**	10
a.s.		Aquatic invertebrates (*D. magna*)	0.0018	Chronic		**3.91**	10

[1] indicate whether Northern of Southern
[2] include critical groups which fail at Step 1.
[3] indicate whether maximum or twa values have been used.
[4] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[5] only required for herbicides

[6] consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used

FOCUS Step 2

Vines total dose 0.3kg a.s./ha 4 x foliar applications

Test substance	N/S[1]	Organism[2]	Toxicity end point (mg/L)	Time scale	PEC[3]	TER	Annex VI Trigger[4]
a.s.		Fish (*O. mykiss*)		Acute		173.6	100
a.s.		Aquatic invertebrates *(D.magna)*		Acute		142.8	100
a.s.		Aquatic invertebrates *(M. bahia)*		Acute		**54.7**	100
a.s.		Fish (*O. mykiss*)		Chronic		**1.49**	10
a.s.		Aquatic invertebrates *(D. magna)*		Chronic		**0.90**	10
a.s.		Algae		Chronic			10
a.s.		Higher plants[5]		Chronic			10
a.s.		Sediment-dwelling organisms[6] *(C. riparius)*		Chronic		25.36	10

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Cereals total dose 0.1 kg a.s./ha 2 x foliar applications based on maximum PEC for the worst case FOCUSsw scenario

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg/L)	PEC[4]	TER	Annex VI trigger[5]
a.s.			Fish (*O. mykiss*)	Chronic			**9.49**	10
a.s.			Aquatic invertebrates (*D. magna*)	Chronic			**5.70**	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 2.
[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

FOCUS Step 3

Vines total dose 0.3 kg a.s./ha 4 x foliar applications based on maximum PEC for the worst case FOCUSsw scenario

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg/L)	PEC[4]	TER	Annex VI trigger[5]
a.s.			Aquatic invertebrates (*M. bahia*)	Acute			**83.9**	100
a.s.			Fish (*O. mykiss*)	Chronic			**2.29**	10
a.s.			Aquatic invertebrates (*D. magna*)	Chronic			**1.37**	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 3.
[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

FOCUS Step 4

Cereals total dose 0.1 kg a.s./ha 2 x foliar applications based on maximum PEC for the worst case FOCUSsw scenario

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point	Buffer zone distance	PEC[4]	TER	Annex VI trigger[5]
		Fish (*O. mykiss*)	Chronic		3		18.18	10
		Aquatic invertebrates (*D. magna*)	Chronic		3		10.91	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 3.
[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

FOCUS Step 4

Vines total dose 0.3 kg a.s./ha 4 x foliar applications based on maximum PEC for the worst case FOCUSsw scenario

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point	Buffer zone distance	PEC[4]	TER	Annex VI trigger[5]
		Aquatic invertebrates (*M. bahia*)	Acute		5		115.1	100
		Fish (*O. mykiss*)	Chronic		16		17.65	10
		Aquatic invertebrates (*D. magna*)	Chronic		16		10.59	10

Bioconcentration		
	Active substance	IN-MM671
$logP_{O/W}$	5.5	3.42
Bioconcentration factor (BCF)[1] ‡	821	483
Annex VI Trigger for the bioconcentration factor	100	100
Clearance time (days) (CT_{50})	Not calculated	Not calculated
(CT_{95})	5.8 d	4.0
Level and nature of residues (%) in organisms after the 14 day depuration phase	0.0 - 4.9	1.0 – 1.3

[1] only required if log $P_{O/W}$ >3.
* based on total ^{14}C or on specific compounds

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

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	> 125	> 197
Preparation[1]	>99.75 a.s.	>100 a.s.

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

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

Cereals total dose 0.1 kg a.s./ha 2 x foliar applications

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	0.25	50
a.s.	Oral	0.4	50
Preparation	Contact	0.5	50
Preparation	Oral	0.5	50

Vines total dose 0.3 kg a.s./ha 4 x foliar applications

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	0.38	50
a.s.	oral	0.6	50
Preparation	Contact	0.75	50
Preparation	oral	0.75	50

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ‡	Formulation	Mortality	47.85 g a.s./ha
Aphidius rhopalosiphi ‡	Formulation	Mortality	131.42 g a.s./ha

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

Cereals total dose 0.1 kg a.s./ha 2 x foliar applications

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
Formulation	*Typhlodromus pyri*	47.85 g a.s./ha	1.78	0.042	2
Formulation	*Aphidius rhopalosiphi*	131.42 g a.s./ha	0.65	0.015	2

[1] indicate distance assumed to calculate the drift rate

Vines total dose 0.3 kg a.s./ha 4 x foliar applications

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
Formulation	*Typhlodromus pyri*	47.85 g a.s./ha	**4.23**	0.284	2
Formulation	*Aphidius rhopalosiphi*	131.42 g a.s./ha	1.54	0.103	2

[1] indicate distance assumed to calculate the drift rate

Extended Laboratory Studies

Species	Life Stage	Test substance, substrate and duration	Dose (g/ha) 14 day application interval	Endpoint	% Effect	Trigger (ESCO RT 2)
Aphidius rhopalosiphi	Adults <48 hr old	Formulation * Vine leaf 48 hours	1 x 75g[1] 4 x 75g[2] 4 x 75g[3]	Mortality (48 hrs exposure) [compared with untreated control]	[1]5.0 [2.5]% [2]0.0 [0]% [3]10.3 [9.8]%	50%
				Reproduction (10-12 day exp.) %parasitised aphids/female[#]	[1]102% [2]133% [3]105%	
Chrysoperla carnea	1st Instar 2-3 days old	Formulation * Vine leaf 20 days (± 3)	1 x 75g[1] 4 x 75g[2] 4 x 75g[3]	Mortality (20 day exp.) [compared with untreated control]	[1]10.2[10.0] % [2]10.0[18.8] % [3]8.0[8.2]%	50%
				Fecundity (0-9 day exp.) %eggs/female/d[#]	[1]81.8% [2]75.4% [3]72.4%	
Orius laevigatus	2nd Instar 4 days old	Formulation * Vine leaf 9 days	1 x 75g[1] 4 x 75g[2] 4 x 75g[3] 3 x 75g[4]	Mortality (9 day exposure) [compared with untreated control]	[1]16.25[10]% [2]2.5[0]% [3]5.0[7.5]% [4]3.75[8.75] %	50%
				Fecundity (11-18 days) %eggs/female/d[#]	[1]138% [2]86.5% [3]-[‡] [4]107%	
Aphidius rhopalosiphi	Adults <48 hr old	Formulation * Wheat plants 72 hours	1 x 50g[1] 3 x 50g[5]	Mortality (72 hrs) [compared with untreated control]	[1]12.0[24]% [5]8.0[6]%	50%
				Reproduction (10-12 days) %parasitised aphids/female[#]	[1]114% [5]71.0%	

*'Proquinazid 200 g/l EC'. [#]Compared to control. [‡]All test females died due to equipment failure.
[1]Fresh residue (0 DAT1). [2]Fresh residue (0 DAT4). [3]Field aged residue (7 DAT4). [4]Fresh residue (0 DAT3).
[5]Fresh residue (0 DAT3).

Field or semi-field tests
Data were submitted from three replicated field studies carried out in vineyards in Germany, Italy and France, investigating the effects of 75 g a.s./ha 'Proquinazid 200 g/l EC' (4 applications at 14 day intervals) on predatory mites. Periodic assessments took place between 4 days before 1st application (4 DBA1) and 31 days after 4th application (31 DAA4). ---------- Maximum %reduction of adults and nymphs in treated plots (relative to the untreated control plots) German study: 20.89% (7 DAA4) Italian study: 27.94% (14 DAA1) (*all consistently below ESCORT 2 trigger value - 50%)* French study: 22.22% (14 DAA1) ---------- %reduction of adults and nymphs in treated plots (relative to the untreated control plots) 28-31 DAA4: German study: 0.95% Italian study: -27.12% (*recovery to untreated control levels by 1 month after final application*) French study: -20.38%

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point[1]
Earthworms			
	a.s.	Acute 14 d	LC_{50} mg > 1000 a.s./kg d.w.soil
	Preparation	Acute	LC_{50} mg > 198.8 mg a.s./kg d.w.soil
	Preparation	Chronic 56 d	NOEC 50.9 mg a.s./kg d.w.soil
	IN-MM671	Acute	LC_{50} mg > 100 mg/kg d.w.soil
	IN-MM986	Acute	LC_{50} mg > 100 mg/kg d.w.soil
	IN-MM991	Acute	LC_{50} mg > 100 mg/kg d.w.soil
	IN-MM671	Chronic	NOEC mg 100 mg/kg d.w.soil
Other soil macro-organisms			
Soil mite	a.s. ‡		
	Preparation		
	Metabolite 1		
Collembola			
	a.s. ‡	Chronic	NOEC mg a.s./kg d.w.soil (mg a.s/ha)
	Preparation		
	Metabolite 1		
Soil micro-organisms			
Nitrogen mineralisation	Formulation		<25% effect at 5.0 mg a.s./kg d.w.soil
	IN-MM671		<25% effect at 0.67 mg a.s./kg d.w.soil
	IN-MM986		<25% effect at 0.67 mg a.s./kg d.w.soil
	IN-MM991		<25% effect at 0.67 mg a.s./kg d.w.soil
Carbon mineralisation	Formulation		<25% effect at 5.0 mg a.s./kg d.w.soil
	IN-MM671		<25% effect at 0.67 mg a.s./kg d.w.soil
	IN-MM986		<25% effect at 0.67 mg a.s./kg d.w.soil
	IN-MM991		<25% effect at 0.67 mg a.s./kg d.w.soil
Field or semi-field tests			

Test organism	Test substance	Time scale	End point[1]
Data were submitted from one 'Litter-bag' study carried out in Germany (bare soil-agricultural situation), conducted according to the recommendations of the 'EPFES' workshop (Lisbon, 2002) --- *1st application 337.5 ml/ha 'Proquinazid 200 g/l EC' (equivalent to 67.5 g a.s./ha) - 15 day interval* *2nd application 750 ml/ha 'Proquinazid 200 g/l EC' (equivalent to 150 g a.s./ha)* *This would be equivalent to the maximum 'peak plateau' dose of proquinazid and IN-MM671 likely to be encountered following the proposed use pattern in vines (maximum dose 75 g a.s./ha)* *Assessments of litter breakdown were carried out 1, 3, 5, 6, 9 and 12 months after the 2nd application* --- *%litter breakdown in treated plots (relative to the untreated control plots) = ± 10%*			

[1] indicate where end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

Toxicity/exposure ratios for soil organisms

Cereals total dose 0.1 kg a.s./ha 2 x foliar applications

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Earthworms					
	a.s. ‡	Acute	0.062	8064	10
	Preparation	Acute	0.062	1603	10
	Preparation	Chronic	0.062	410	5
	IN-MM671	Acute	0.024#	2083	10
	IN-MM671	Chronic	0.024#	2083	5
	IN-MM986	Acute	0.019	2632	10
	IN-MM991	Acute	0.005	10000	10
Other soil macro-organisms					
Soil mite	a.s. ‡				
	Preparation				
	Metabolite 1				
Collembola	a.s. ‡				
	Preparation				
	Metabolite 1				

[1] to be completed where first Tier triggers are breached
[2] indicate which PEC soil was used (e.g. plateau PEC)
[#] Peak plateau PECsoil used for this metabolite (DT50 > 365 days)

Vines total dose 0.3 kg a.s./ha 4 x foliar applications

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Earthworms					
	a.s. ‡	Acute	0.164	3049	10
	Preparation	Acute	0.164	606	10
	Preparation	Chronic	0.164	155	5
	IN-MM671	Acute	0.113[#]	442	10
	IN-MM671	Chronic	0.113[#]	442	5
	IN-MM986	Acute	0.019	862	10
	IN-MM991	Acute	0.005	3333	10
Other soil macro-organisms					
Soil mite	a.s. ‡				
	Preparation				
	Metabolite 1				
Collembola	a.s. ‡				
	Preparation				
	Metabolite 1				

[1] to be completed where first Tier triggers are breached
[2] indicate which PEC soil was used (e.g. plateau PEC)
[#] Peak plateau PECsoil used for this metabolite (DT50 > 365 days)

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)
Preliminary screening data

Post-emergence:
Results OECD 208 post-emergence growth test conducted with 'Proquinazid 200g/l EC' at 0.375 l/ha (75 g a.s./ha) were presented.
Phytotoxic symptoms <35% in 6 different crop species (4 dicots + 2 monocots).
In addition, as part of the efficacy submission, results were presented of 16 European field tests (non-GLP) to observe the phytotoxicity of 'Proquinazid 200 g/l EC' (at doses of 20-200 g a.s./ha) applied post emergence to 7 different dicot crops.
No phytotoxicity was seen in any of the trials.

Pre-emergence:
As part of the efficacy submission, data were submitted from a non-GLP study (3 non-replicated sites) to examine the effects on succeeding crops from a field application of 'Proquinazid 200 g/l EC' applied at 100 g a.s./ha to a winter wheat crop (1.25 x maximum individual dose – vines). 7-15 months after application a range of crops (2 cereals and 5 dicot crops) were sown into the previously treated area.
No phytotoxicity was seen in the 7 succeeding crops throughout the growing season.

As up to 15 months elapsed between application and planting of some crops, peak plateau PECsoil concentrations would have been achieved for the three soil metabolites (IN-MM671, IN-MM986 and IN-MM991). Therefore, the risk to non-target plants from the metabolites would have been covered by the application of 'Proquinazid 200 g/l EC'.

Details were also provided for a 1995 greenhouse 'herbicidal activity' study in which use of Proquinazid 200g/l EC applied pre or post emergence at 400g a.s./ha to a range of monocot and dicot non-crop plant species resulted in no phytotoxic effects.

Effects on biological methods for sewage treatment (Annex IIA 8.7)

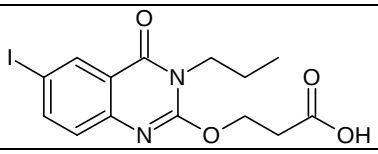
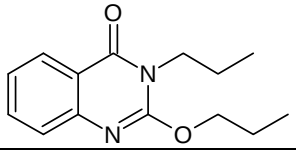
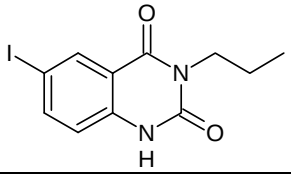
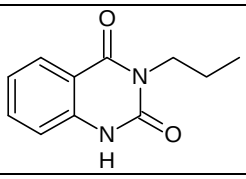
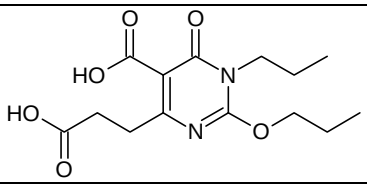
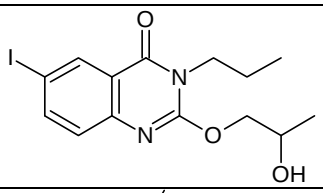
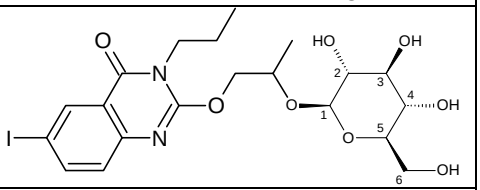
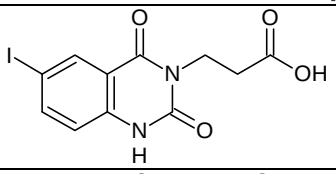
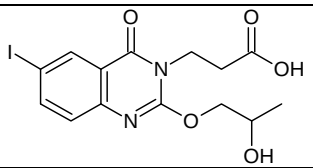
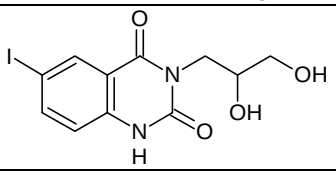
Test type/organism	end point
Activated sludge	Not tested
Pseudomonas sp	Not tested

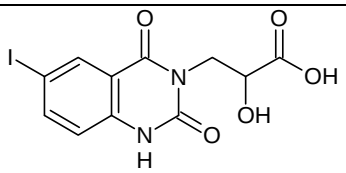
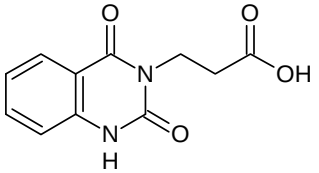
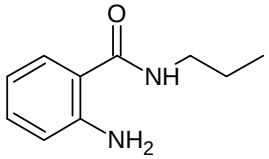
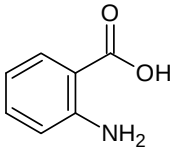
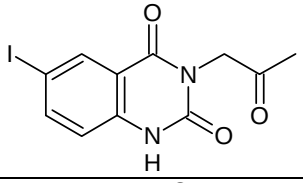
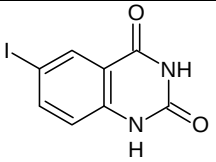
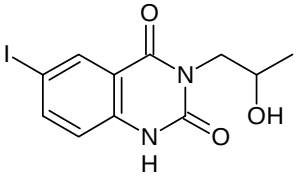
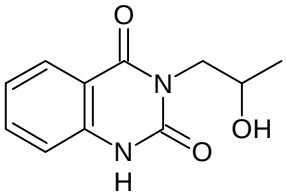
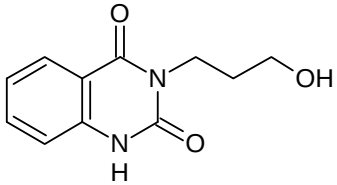
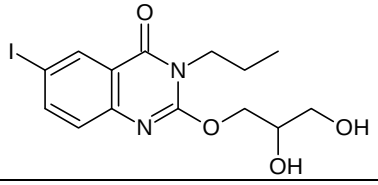
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

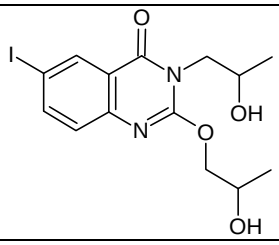
	RMS/peer review proposal
Active substance	**Active substance (proquinazid):** Should carry the 'N' symbol and 'Dangerous for the environment', plus the following risk phrases: **R50** *'Very toxic to aquatic organisms'* **R53** *'May cause long-term effects in aquatic environment.'* **S35** *'This material and its container must be disposed of in a safe way''* **S57** *'Use appropriate containment to avoid environmental contamination'.*

	RMS/peer review proposal
Preparation	**Formulation ('Proquinazid 200 g/l EC':** Should carry the 'N' symbol and 'Dangerous for the environment', plus the following risk phrases: **R51** *'Toxic to aquatic organisms'* **R53** *'May cause long-term effects in aquatic environment.'* **S35** *'This material and its container must be disposed of in a safe way''* **S57** *'Use appropriate containment to avoid environmental contamination'.*

B. USED COMPOUND CODE(S)

Code/Trivial name	Chemical name*	Structural formula
IN-MU210	3-[(6-iodo-4-oxo-3-propyl-3,4-dihydroquinazolin-2-yl)oxy]propanoic acid	
IN-MM671	2-propoxy-3-propylquinazolin-4(3*H*)-one	
IN-MM986	6-iodo-3-propylquinazoline-2,4(1*H*,3*H*)-dione	
IN-MM991	3-propylquinazoline-2,4(1*H*,3*H*)-dione	
IN-MT884	4-(2-carboxyethyl)-6-oxo-2-propoxy-1-propyl-1,6-dihydropyrimidine-5-carboxylic acid	
IN-MW977	2-{[(2*RS*)-2-hydroxypropyl]oxy}-6-iodo-3-propylquinazolin-4(3*H*)-one	
IN-MW977 glucose conjugates	(2*RS*)-1-[(6-iodo-4-oxo-3-propyl-3,4-dihydroquinazolin-2-yl)oxy]propan-2-yl β-D-glucopyranoside	
IN-MU715	3-(6-iodo-2,4-dioxo-1,4-dihydroquinazolin-3(2*H*)-yl)propanoic acid	
IN-MY788	3-[2-{[(2*RS*)-2-hydroxypropyl]oxy}-6-iodo-4-oxoquinazolin-3(4*H*)-yl]propanoic acid	
IN-NA251	3-[(2*RS*)-2,3-dihydroxypropyl]-6-iodoquinazoline-2,4(1*H*,3*H*)-dione	

IN-NA252	(2*RS*)-2-hydroxy-3-(6-iodo-2,4-dioxo-1,4-dihydroquinazolin-3(2*H*)-yl)propanoic acid	
IN-NC147	3-(2,4-dioxo-1,4-dihydroquinazolin-3(2*H*)-yl)propanoic acid	
IN-NC146	2-amino-*N*-propylbenzamide	
Anthranilic acid	2-aminobenzoic acid	
IN-NA250	6-iodo-3-(2-oxopropyl)quinazoline-2,4(1*H*,3*H*)-dione	
IN-MW398	6-iodoquinazoline-2,4(1*H*,3*H*)-dione	
IN-MW397	3-[(2*RS*)-2-hydroxypropyl]-6-iodoquinazoline-2,4(1*H*,3*H*)-dione	
IN-MT712	3-(2-hydroxypropyl)quinazoline-2,4(1*H*,3*H*)-dione	
IN-MT711	3-(3-hydroxypropyl)quinazoline-2,4(1*H*,3*H*)-dione	
IN-MY340	2-{[(2*RS*)-2,3-dihydroxypropyl]oxy}-6-iodo-3-propylquinazolin-4(3*H*)-one	

IN-MY341	3-[(2*RS*)-2-hydroxypropyl]-2-{[(2*RS*)-2-hydroxypropyl]oxy}-6-iodoquinazolin-4(3*H*)-one	

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

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DFR	dislodgeable foliar residue
DM	dry matter
DT50	period required for 50 percent disappearance (define method of estimation)
DT90	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC50	effective concentration (biomass)
EC50	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate/effective rate, median
ErC50	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice

GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
H	Henry's Law coefficient (calculated as a unitless value) (see also K)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
Kdoc	organic carbon linear adsorption coefficient
kg	kilogram
KFoc	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC50	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD50	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MC	moisture content
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter content

Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PECair	predicted environmental concentration in air
PECgw	predicted environmental concentration in ground water
PECsed	predicted environmental concentration in sediment
PECsoil	predicted environmental concentration in soil
PECsw	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pKa	negative logarithm (to the base 10) of the dissociation constant
Pow	partition coefficient between n-octanol and water
PPE	personal protective equipment
ppm	parts per million (10-6)
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
t1/2	half-life (define method of estimation)
TER	toxicity exposure ratio
TERA	toxicity exposure ratio for acute exposure
TERLT	toxicity exposure ratio following chronic exposure
TERST	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDP	uridine diphosphate–glucuronyltransferase
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year