Dossier According to Directive 91/414/EEC

Plant Protection Product

Requiem® EC (QRD 452)

Terpenoid blend (α-terpinene, ρ-cymene, d-limonene) QRD 460

Product for insect pest control developed from plant extracts of *Chenopodium ambrosioides* near *ambrosioides*

Document MIII, Section 6

ECOTOXICOLOGY

Table of Contents

IIIA 10 ECOTOXICOLOGICAL STUDIES OF THE PLANT PROTECTION PRODUCT

AgraQuest Inc. has submitted this application for approval of the new active substance QRD 460 and its product, This section of the Annex III Dossier is addressed using primarily information already presented in the Annex II Section 6 and is summarised, accordingly.

Terpenoid Blend (α-terpinene, p-cymene, and d-limonene) QRD 460 is a new active substance developed by AgraQuest Inc. based originally on naturally occurring extract of the plant species *Chenopodium ambrosioides* near *ambrosioides* for use as an insecticide plant protection product. The product is Requiem® EC (QRD 452) an emulsifiable concentrate which is foliar applied to control common insect pests of protected and open field crops. It contain 16.75 % (w/w) of the active substance: Terpenoid blend (α-terpinene, p-cymene, d-limonene) QRD 460.

To defend themselves against herbivores and pathogens, plants naturally release a variety of volatiles including various alcohols, terpenes and aromatic compounds. These volatiles can deter insects or other herbivores from feeding, can have direct toxic effects on pests, or they may be involved in recruiting predators and parasitoids in response to feeding damage (Ashour *et al*. 2010). They may also be used by the plants to attract pollinators, protect plants from disease, or they may be involved in interplant communication. As these properties have been known and observed for a very long time, it is a natural progression that three such terpenes, α-terpinene, p-cymene, and d-limonene, have been identified as candidates for biopesticidal use. In the original plant extract the three terpene compounds in combination are the source of insecticidal activity: as this naturally occurring combination is the key active moiety, they are considered and termed to be one active substance. This consideration was agreed at the DG SANCO Phytopharmaceutical Standing Committee meeting 26-27 November 2009 for QRD 420, which contains the same active substance as QRD 460.

The original plant extract (QRD 406) was registered by US EPA as a biopesticide in April 2008. The initial active substance and product was based on a plant extract of *Chenopodium ambrosioides* near *ambrosioides*. The essential oil was harvested from the plant biomass using steam distillation. Variability in growing conditions for the plants meant this active substance suffered from variability in the concentration of the three constituent active terpenes and so an alternative, QRD 460 was developed which is an optimized blend of the three terpenes that reflects the proportions found in the original plant extract QRD 406.

AgraQuest Inc. has submitted this application for approval of the new active substance QRD 460 and its product, QRD 452 respectively, for registration in the EU with ctgb Netherlands as the Rapporteur Member State. It is an insecticide for use on tomatoes and peppers in glasshouses and cucurbits in glasshouses and field at a maximum application rate of 1.523 kg as/ha up to 3 times with a 7 day interval between treatments.

Table 6-1: EU Critical GAP for QRD 460 use on Tomatoes, Peppers and Cucurbits

Region	Outdoor/ Protected	Max. No. of Applications	Application Interval (days)	Max. Application		Minimum PHI (days)
				Rate (kg as/ha)	Water (L/ha)	
N EU	Protected	3	7	0.381 – 1.523	400 - 1000	0
S EU	Protected	3	7	0.381 – 1.523	400 - 1000	0
S EU	Outdoor	3	7	0.762 – 1.523	400 - 1000	0

The mode of action of the product is considered non-toxic. Based on laboratory and field trial observations, the mechanism for controlling insect pests is considered to be through degradation of soft insect cuticles resulting in a disruption of insect mobility and respiration. This is considered to occur by direct contact and localized fumigant action. For further details, please refer to document MIII, Section 7, Point 6.

It is noteworthy that these terpenes, α-terpinene, p-cymene, and d-limonene, are commonly used as fragrances and flavourings (Joint FAO/WHO Expert Committee on Food Additives & WHO Technical Report Series 928.). They are present in abundance in many herb plants, and are common in many other edible plants such as citrus fruits, tomatoes, celery and carrots, with various functions as secondary metabolites (Ashour *et al*, 2010). Consequently they are a ubiquitous part of both human and animals' natural diet and it is reasonable to expect regular contact with them in the environment without any concern.

All three terpenes are also found, to a greater or lesser extent, in the following EU registered or pending active substances: tea tree oil, thyme oil, orange oil, citronella, spearmint oil, tagetes (marigold) oil.

Due to the well known volatile nature of Terpenoid blend (α-terpinene, ρ-cymene, d- limonene) QRD 460, the fact that all three terpenoids occur naturally and are ubiquitous and normal exposure presents no significant risk to humans, animals or the environment, so the plant protection use proposed here adds nothing of significance to the natural exposure, it is believed that safety is confirmed and so no additional data is considered necessary.

From the Annex II Physical Chemical properties Section 1, the Metabolism and Residue behaviour in Section 4 and the Environmental Fate Section 5, it is clear that QRD 452 does not result in residues when applied and does not remain in the environment for any significant time. It is both volatilised to and breaks down in air, rapidly, in a matter of hours. This means that exposure levels to ecotoxicologically relevant species are expected to be minimal or non-existent from the plant protection use of QRD 452.

However, it is perfectly possible that exposure may occur from the other many natural sources of the three terpenoid constituents of QRD 452, α-terpinene, ρ-cymene, d-limonene. They are present in abundance in many herb plants, and are common in many other edible plants such as citrus fruits, tomatoes, celery and carrots, with various functions as secondary metabolites (Ashour,. *et al*, (2010). Consequently they form a significant part of both human and animals', birds and fish, insects and other non-target fauna's natural diet and also it is natural to come into contact with them from the environment via touch and in the air, without any concern. The three terpenes dissipate rapidly and hence their characteristic smell also diminishes rapidly as they break down.

All three terpenes are also found, to a greater or lesser extent, in the following EU registered or pending active substances: tea tree oil, thyme oil, orange oil, citronella, spearmint oil, tagetes (marigold) oil.

As a result of their nature, it was not possible to calculate predicted environmental concentrations of the three active constituents of QRD 452 as would be the normal procedure for a pesticide. This is because they breakdown and dissipate primarily in air, too rapidly. As such the risk to relevant species is considered too small to realistically quantify. Similarly it is not possible to calculate TERs or ETEs as there is no meaningful dietary exposure and no figure for concentration in the diet from use of QRD 452 except zero.

Tests were performed on the QRD 452 constituents on various species to demonstrate the lack of toxicity and it is clear that the plant protection use of QRD 452 does not raise any concerns. The results of the studies generally demonstrate that no effects were seen at the limit doses and so it can be accepted that as these doses far exceed any possible level that species could realistically come into contact with from the plant protection use of QRD 542, acceptable margins of safety are there and no concern with respect to risk is raised.

To aid evaluation of the dossier, the code designations are described so that it is clear which test substance was used for each study. All substances listed are considered substantially equivalent.

Code Designations

The various AgraQuest code designations that relate to the active substance, products and the submitted documents are as follows:

QRD 406 = *Chenopodium ambrosioides* near *ambrosioides* plant extract technical grade active ingredient (tgai) – consisting of the three terpenes as the active component plus plant derived impurities. Three terpenes comprise approximately 68% of QRD 406.

QRD 400 = formulated EC product with 25% plant extract (QRD 406) active ingredient, 75% other formulants (Also known as FACIN 25EC in some reports and registered in the USA as Requiem® 25EC and Metronome™.) The three terpenes in QRD 400 comprise approximately 17%.

QRD 420 = blended tgai using the three terpenes in the same concentrations as found in QRD 406 with plant derived impurities replaced with canola oil. The three terpenes comprise approximately 67% of QRD 420.

QRD 416 = formulated EC product with 25% blended (QRD 420) a.i., 75% other formulants (same formulants in the same concentrations as QRD 400). The three terpenes comprise approximately 16.75 % of QRD 416.

QRD 452 = QRD 416 – due to a code designation error, the product was re-coded as QRD 452. There are a few studies that reference QRD 416, but the composition is identical to QRD 452. (Also known and registered in the USA as Requiem® EC and Metronome™ EC). The concentration of the three terpenes in QRD 416 and QRD 452 is 16.75%.

QRD 460 = Blended tgai without canola oil. This contains only the three terpenes. The proportions of the three terpenes are essentially the same as the plant extract tgai minus plant derived impurities. So, less QRD 460 is required in Requiem® EC (QRD 452), 16.75% instead of 25%. The percentage of each terpene in QRD 452 and QRD 400 are the same.

IIIA 10.1 Effects on birds

IIIA 10.1.1 Acute toxicity exposure ratio (TERA) for birds

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Avian (IIA 8.1.1)					
Northern Bobwhite Quail	Acute oral, single dose	QRD 406 plant extract a.s.	LC_{50} > 2250 mg/kg	US-EPA & OPPTS Number 850.2100	[redacted] & , 2007

Estimated Theoretical Exposure calculations are usually based on dietary exposure of birds to the plant protection product based on residues on and in the plants. As it has been shown in Section 4 Metabolism and Residues that meaningful measurable residues do not occur on the crops from the use of QRD 452 due to its rapid volatilisation, it is not possible to estimate C, the concentration in food, as anything other than zero. Coupled with the predominant glasshouse use, it is more likely that any exposure could be from natural sources rather than QRD 452. Therefore an ETE and hence TER cannot be reliably estimated.

As the levels of the active substance QRD 460 found on plants after application of the product QRD 452 are expected to be minimal due to the rapid volatilisation of the actives, thus exposure of avian species to QRD 452 is not expected to be significant via the oral route or due to contact with treated foliage or fruits. Also due to its rapid volatilisation from water, significant exposure is unlikely to occur to avians from drinking treated water.

The only likely exposure could be from air and it is proposed that the QRD 460 degrades in air completely in less than 48 hours (longest predicted DT_{100} for ρ-cymene was predicted to be 46.4 hours in air, the other two terpene components, much shorter) and so this is also an unlikely route of significant exposure, especially with the main use being in glass houses.

In one acute study on the Northern Bobwhite Quail, a lack of toxicity was demonstrated with the result of an LC_{50} > 2250 mg/kg. Mammalian studies from the Toxicology section also suggest a low level of toxicity to other species.

A simplistic comparison of the above LC_{50} with the $PEC_{greenhouse\ air}$ = 0.043 mg/L calculated in the Environmental Fate section is difficult to conclude from as a bird inhalation study would be needed to give a more meaningful comparison. However a mammalian inhalation study has been performed on QRD 460 and gave the following result: acute inhalation LC_{50} of QRD 460 is greater than 5.30 mg/L in male and female albino rats. Clearly this gives more than a 120 fold safety factor and indicates that even with a very conservative overestimate of exposure PEC calculation, the risk to birds is not of concern.

It is concluded that there is no significant risk to birds from the use of QRD 452 and that further investigation with studies or calculations of ETEs or TERs are not required as they would add nothing more to this conclusion.

IIIA 10.1.2 Short-term toxicity exposure ratio (TER_{ST}) for birds

As the levels of the active substance QRD 460 found on plants after application of the product QRD 452 are expected to be minimal due to the rapid volatilisation of the actives, thus exposure of avian species to QRD 452 is not expected to be significant via the oral route or due to contact with treated foliage or fruits. Also due to its rapid volatilisation from water, significant exposure is unlikely to occur to avians from drinking treated water.

It is concluded that there is no significant risk to birds from the use of QRD 452 and calculation of a short-term toxicity exposure ratio for birds is unwarranted.

IIIA 10.1.3 In the case of baits, the concentration of active substance in the bait in mg/kg

QRD 452 is not applied as a bait.

IIIA 10.1.4 In the case of pellets, granules, prills or treated seed

IIIA 10.1.4.1 Amount of the active substance in or on each pellet, granule, prill or treated seed

QRD 452 is not applied as a pellet, granule, prill or as a seed treatment.

IIIA 10.1.4.2 Proportion of the LD_{50} for the active substance in 100 particles and per gram of particles

QRD 452 is not applied as a pellet, granule, prill or as a seed treatment.

IIIA 10.1.5 In the case of pellets, granules, and prills, their size and shape

QRD 452 is not applied as a pellet, granule, prill or as a seed treatment.

IIIA 10.1.6 Acute oral toxicity of the preparation to the more sensitive of the species identified in tests with the active substance

QRD 452 is not applied as a pellet, granule, prill or as a seed treatment.

IIIA 10.1.7 Supervised cage or field trials

QRD 452 is not applied as a pellet, granule, prill or as a seed treatment.

IIIA 10.1.8 Acceptance of bait, granules or treated seeds by birds (palatability test)

QRD 452 is not applied as a pellet, granule, prill or as a seed treatment.

IIIA 10.1.9 Effects of secondary poisoning

QRD 452 is not applied as a pellet, granule, prill or as a seed treatment.

IIIA 10.2 Effects on aquatic organisms

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Fish (IIA 8.2.1.2)					
Fathead minnow (*Pimephales promelas*)	Acute , 96 hr flow-through	QRD 460 a.s.	LC_{50} > 1.17 mg /L NOEC 1.17 mg /L.	OECD 203	[redacted], 2011a

Estimated Theoretical Exposure calculations are usually based on exposure of aquatic species to the plant protection product based on residues in water.

It has been shown in Section 5 Environmental fate and Behaviour that the three test items α-terpinene, ρ-cymene, and d-limonene were volatilized from the natural water test system rapidly with DT_{50}s of 4.1, 3.0, and 11.2 hours and DT_{90}s of 13.7, 37.4 and 10.0 hours for α-terpinene, ρ-cymene, and d-limonene, respectively. This means that a DT_{100} could be proposed for QRD 460 and its product QRD 452 of < 48 hours. QRD 452 is not persistent.

This means that exposure of aquatic organisms to QRD 452 only occurs for a matter of hours, if at all, as the plant protection product rapidly volatilises into the air. It is unlikely that any exposure will reliably occur and if it does, it could be more from natural sources (in the plants around the aquatic systems) rather than the QRD 452 plant protection use, and as such has never generated concern. It is not possible to come up with a realistic PEC in water because of the speed of removal from the aquatic system and hence PERs cannot be reliably estimated as the levels of the components in QRD 452 are too low.

In one acute flow through study on the Fathead minnow, a lack of toxicity was demonstrated with the result of an LC_{50} > 1.17 mg /L and a NOEC ≥ 1.17 mg /L, the highest limit tested. It should also be noted that experimentally, the active components in QRD 452 are not particularly soluble in water and so this limits the highest concentration available for testing. For this reason, the real LC_{50} is likely to be considerably higher.

Mammalian studies from the Toxicology section and the avian study also suggest a low level of toxicity to other species. Combined with the other studies in this section, it is suggested that additional work is unnecessary as the toxicity is sufficiently low and of no real concern.

It is concluded that there is no significant risk to aquatic species from the use of QRD 452 and that further investigation with studies or calculations of TERs are not required as they would add nothing more to this conclusion.

IIIA 10.2.1 Toxicity exposure ratios for aquatic species

IIIA 10.2.1.1 TER_A for fish

A DT_{100} is proposed for QRD 452 of <48 hours in water and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless.

Therefore there is no significant acute risk to aquatic species and no TER is required.

IIIA 10.2.1.2 TER_{LT} for fish

As a DT_{100} is proposed for QRD 452 of <48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.2.1.3 TER_A for *Daphnia*

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Invertebrates (IIA 8.3.1.1)					
Daphnia magna	Acute, 24 hr and 48 hr flow-through	QRD 460 a.s.	24- and 48-hour EC_{50} > 1.04 mg/L. 48-hour NOEC = 0.132 mg/L	OECD 202	[redacted], 2011b

In one acute flow through study on *Daphnia magna*, low toxicity was demonstrated with the result of an EC_{50} > 1.04 mg/L and a NOEC = 0.132 mg/L.

A DT_{100} is proposed for QRD 452 of <48 hours in water demonstrating that QRD 452 is not persistent and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless.

These results and the fact that mammalian studies from the Toxicology section, the avian study and other aquatic studies (showing a low level of toxicity to other species), combined with the other studies in this section, suggest that additional work is unnecessary as the toxicity is sufficiently low and of no real concern.

It is concluded that there is no significant risk to *Daphnia* from the use of QRD 452 and that further investigation with studies or calculations of TERs are not required as they would add nothing more to this conclusion.

Therefore there is no significant acute risk to aquatic species and no TER is required.

IIIA 10.2.1.4 TER_{LT} for *Daphnia*

As a DT_{100} is proposed for QRD 452 of <48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered and therefore no TER is required.

IIIA 10.2.1.5 $TER_{A or F}$ for an aquatic insect species

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Sediment Dwellers (IIA 8.5.1)					
Midge larvae (*Chironomus riparius*)	Acute, 48 hr flow-through	QRD 460 a.s.	48-hour EC_{50} = 0.86 mg/L 48-hour NOEC = 0.360 mg/L	OECD 202	[redacted], 2011d

In one acute flow through study on the sediment dwelling aquatic insect species *Chironomus riparius*, low toxicity was demonstrated with the result of a 48-hour EC_{50} = 0.86 mg/L and a 48-hour NOEC = 0.360 mg/L .

A DT_{100} is proposed for QRD 452 of <48 hours in water demonstrating that QRD 452 is not persistent and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless.

Clearly any exposure of aquatic insect species to QRD 452 will be brief and transient and not expected to last as long as the study test exposure length.

These results and the fact that mammalian studies, the avian study and other aquatic studies (showing a low level of toxicity to other species), suggest that additional work is unnecessary as the toxicity is sufficiently low and of no real concern.

It is concluded that there is no significant risk to Midge larvae from the use of QRD 452 and that further investigation with studies or calculations of TERs are not required as they would add nothing more to this conclusion.

Therefore there is no significant acute risk to aquatic insect species and no TER is required.

IIIA 10.2.1.6 TER_{LT} for an aquatic insect species

As a DT_{100} is proposed for QRD 452 of < 48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.2.1.7 TER_A for an aquatic crustacean species

A DT_{100} is proposed for QRD 452 of < 48 hours in water and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless.

Therefore there is no significant acute risk to aquatic species and no TER is required.

IIIA 10.2.1.8 TER_{LT} for an aquatic crustacean species

As a DT_{100} is proposed for QRD 452 of <48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.2.1.9 TER_A for an aquatic gastropod mollusc species

A DT_{100} is proposed for QRD 452 of <48 hours in water and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless.

Therefore there is no significant acute risk to aquatic gastropod mollusk species and no TER is required.

IIIA 10.2.1.10 TER_{LT} for an aquatic gastropod mollusc species

As a DT_{100} is proposed for QRD 452 of < 48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.2.1.11 TER_{LT} for algae

As a DT_{100} is proposed for QRD 452 of < 48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.2.2 Acute toxicity (aquatic) of the preparation

IIIA 10.2.2.1 Fish acute toxicity LC50, freshwater, cold-water species

Please see 10.2.1.

IIIA 10.2.2.2 Acute toxicity (24 & 48 h) for *Daphnia* preferably *Daphnia magna*

Please see 10.2.1.

IIIA 10.2.2.3 Effects on algal growth and growth rate

Please see 10.2.1.

IIIA 10.2.2.4 Marine or estuarine organisms acute toxicity LC_{50}/EC_{50}

This is not an EC data requirement.

IIIA 10.2.2.5 Marine sediment invertebrates, acute toxicity LC_{50}/EC_{50}

This is not an EC data requirement.

IIIA 10.2.3 Microcosm or mesocosm study

As a DT_{100} is proposed for QRD 452 of <48 hours in water and the product volatilises into air rapidly, no microcosm or mesocosm studies are triggered.

IIIA 10.2.4 Residue data in fish (long-term)

As a DT_{100} is proposed for QRD 452 of < 48 hours in water and the product volatilises into air rapidly and breaks down rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.2.5 Chronic fish toxicity data

IIIA 10.2.5.1 Chronic toxicity (28 day exposure) to juvenile fish

As a DT_{100} is proposed for QRD 452 of < 48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered.

IIIA 10.2.5.2 Fish early life stage toxicity test

As a DT_{100} is proposed for QRD 452 of < 48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.2.5.3 Fish life cycle test

As a DT_{100} is proposed for QRD 452 of < 48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.2.6 Chronic toxicity to aquatic invertebrates

IIIA 10.2.6.1 Chronic toxicity in *Daphnia magna* (21-day)

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Invertebrates (IIA 8.3.2.1)					
Daphnia magna	Chronic, 21-day, flow-through	QRD 460 a.s.	EC_{50} reproduction = 0.308 mg/L LOEC = 0.173 mg/L. NOEC = 0.214 mg/L	OECD 211.	[redacted], 2011c

In one chronic flow through study on *Daphnia magna*, low toxicity was demonstrated with the result of an EC_{50} for reproduction = 0.308 mg/Land a NOEC = 0.214 mg/L.

A DT_{100} is proposed for QRD 452 of <48 hours in water demonstrating that QRD 452 is not persistent and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless.

These results and the fact that mammalian studies from the Toxicology section, the avian study and other aquatic studies (showing a low level of toxicity to other species) combined with the other studies in this section, suggest that additional work is unnecessary as the toxicity is sufficiently low and of no real concern.

It is concluded that there is no significant acute or chronic risk to *Daphnia* from the use of QRD 452 and that further investigation with studies or calculations of TERs are not required as they would add nothing more to this conclusion.

Therefore there is no significant chronic risk to aquatic species and no TER is required.

IIIA 10.2.6.2 Chronic toxicity for a representative species of aquatic insects

As a DT_{100} is proposed for QRD 452 of <48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.2.6.3 Chronic toxicity for a representative species of aquatic gastropod molluscs

As a DT_{100} is proposed for QRD 452 of <48 hours in water and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.2.7 Accumulation in aquatic non-target organisms

This is not an EC data requirement.

IIIA 10.3 Effects on terrestrial vertebrates other than birds

IIIA 10.3.1 Toxicity exposure ratios for terrestrial vertebrates other than birds

A DT_{100} is proposed for QRD 452 of < 48 hours in soil and water and dissipates equally rapidly from plant surfaces leaving little to no residue and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless.

Therefore, the realistic exposure of terrestrial vertebrates is not going to be significant in the short time of exposure and as such, no meaningful TER can be calculated.

IIIA 10.3.1.1 Acute toxicity exposure ratio (TER_A)

Assuming exposure from air or directly from the application of QRD 452 but not from dietary means (as residues on potential terrestrial vertebrate foodstuffs are insignificant in a very short time), an inhalation study has been performed with QRD 460.

Direct contact can be addressed with the acute dermal test (IIA 5.2.2), where the LD_{50} of QRD 460 is greater than 5050 mg/kg in male and female rats thus demonstrating a lack of toxicity at the highest limit dose and thus any risk from application of diluted QRD 452 would be even less.

A simplistic comparison of the acute inhalation LC_{50} of QRD 460 > 5.30 mg/L in male and female albino rats (IIA 5.2.3) with the PEC $_{greenhouse\ air.}$ = 0.043 mg/L calculated in the Environmental Fate section gives more than a 120 fold safety factor and indicates that even with a very conservative overestimate of exposure/PEC calculation, the risk to terrestrial mammals from air is not of concern. The glass house PEC is expected to be higher than that in the field and hence is already a worst case.

Where inhalation occurs, the flowing is concluded from the toxicokinetics section of the Annex II dossier; In summary, whilst there are no ADME data for QRD 460, published data exist for its terpene components p-cymene and d-limonene and these data indicate the terpenes have similar pathways of metabolism in animals and humans. It is also reasonable to assume that α-terpinene will be metabolized in essentially the same manner as p-cymene and d-limonene. Following an oral dose, the components of QRD 460 are rapidly and well absorbed from the gastrointestinal tract and metabolites are excreted, mostly via urine, within 48 hours (with the major part excreted within 24 hours). The amount of d-limonene absorbed via the oral route is similar in different species; reported values range from 50-96% in rats, guinea-pigs, hamsters and dogs, whilst those in human male volunteers are reported as 50-80% (Kodama *et al*, 1976; Igimi *et al*, 1974). Absorption via the inhalation route is also rapid; the percentage absorbed is reported by Falk *et al* 1990 to average 65%. Similar absorption values are reported for p-cymene (70-80%) in rats and guinea pigs with recovery within 48 hours. Given the similar structure and properties of α-terpinene, absorption values are likely to be comparable. The available data indicate the components of QRD 460 are readily metabolised to materials which are rapidly excreted within 48 hours.

Thus it can be concluded that exposure to terrestrial vertebrates will be minimal as QRD 452 volatilises to air rapidly but where it does occur via inhalation or direct contact, the toxicity of QRD 452 is sufficiently low to cause no concern and the risk is acceptable. Dietary exposure would be minimal as fully explained in the Section 4 Metabolism and Residue summary and so requires no further consideration.

IIIA 10.3.1.2 Short-term toxicity exposure ratio (TER_{ST})

The product QRD 452 volatilises into air rapidly and as a DT_{100} is proposed for QRD 452 of < 48 hours in water, soil and via animal metabolism and residues in plants are sufficiently low to be undetectable after 48 hours therefore no further short term studies or short risk assessment is triggered. No TER is required.

IIIA 10.3.1.3 Long-term toxicity exposure ratio (TER_{LT})

The product QRD 452 volatilises into air rapidly and as a DT_{100} is proposed for QRD 452 of < 48 hours in water, soil and via animal metabolism and residues in plants are sufficiently low to be undetectable after 48 hours therefore no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.3.2 Effects to terrestrial vertebrates other than birds, where the required information is not provided by testing in accordance with points 5 and IIIA 7, and where exposure is likely

IIIA 10.3.2.1 Acute oral toxicity of the preparation

This is fully addressed under Point 10.3.1

IIIA 10.3.2.2 Acceptance of bait, granules or treated seeds by terrestrial vertebrates (palatability test)

Not relevant as QRD 452 is not a bait, granule or seed treatment.

IIIA 10.3.2.3 Effects of secondary poisoning

QRD 452 dissipates into air within 48 hours of application and breaks down as rapidly and so secondary poisoning is rather unlikely.

IIIA 10.3.3 Supervised cage or field trials or other appropriate studies

None required.

IIIA 10.4 Effects on bees

IIIA 10.4.1 Hazard Quotients for bees

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Bees (IIA 8.7.2)					
01/ Honey Bee *Apis mellifera*	Acute contact, 48hr	QRD 420 a.s.+ canola oil	LD_{50} > 100 µg a.i./bee	OECD 214	[redacted] & 2009a
02/ Honey Bee *Apis mellifera*	Acute contact, 48hr	QRD 452 16.75% EC formulation	LD_{50} > 100µg a.i./bee.	OECD 214	[redacted] & 2009b

Two studies on bees have been performed, one on an older formulation QRD 420 and one on the current formulation submitted for registration here, QRD 452.

IIIA 10.4.1.1 Oral exposure Q_{HO}

As the potential for oral exposure is minimal as QRD 452 volatilizes into air leaving no measurable residues on crops or potential bee foodstuffs (such as pollen) within a very short time (less than 48 hours) it was not considered necessary to test the bees via the oral pathway.

IIIA 10.4.1.2 Contact exposure Q_{HC}

As dermal contact is more potentially likely, two studies have been done on two formulations and the results were consistent with both.

The acute risk to bees from contact is expressed as a Hazard Quotient calculated by the following formula: (single application rate in g/ha, LD_{50} in µg a.i./bee)

Hazard Quotient Q_{HC} = application rate / LD_{50}

Table 10.4.1.2-1 Risk to honey bees from contact exposure to formulated product (QRD 452 and QRD 420) containing QRD 460 in tomatoes, peppers, melons and curcubits as Hazard Quotient Q_{HC}

Test Substance	Exposure route	Application rate (g a.s./ha)	Endpoint	Value (µg a.i./bee)	Q_{HC}
QRD 420	contact	1523	LD_{50}	>100	15.23
QRD 452	contact	1523	LD_{50}	>100	15.23

The resulting Hazard Quotients are both clearly below the trigger of 50 indicating low risk to honey bees after the use of QRD 452.

IIIA 10.4.2 Acute toxicity of the preparation to bees

IIIA 10.4.2.1 Acute oral toxicity

Please see 10.4.1

IIIA 10.4.2.2 Acute contact toxicity

Please see 10.4.1

IIIA 10.4.3 Effects on bees of residues on crops

As there are no easily measurable residues on crops due to the rapid volatilisation and break down in air of QRD 452, no effects would be expected.

IIIA 10.4.4 Cage tests

Not required as not triggered.

IIIA 10.4.5 Field tests

Not required as not triggered.

IIIA 10.4.6 Investigation of special effects

IIIA 10.4.6.1 Larval toxicity

Not required as not triggered.

IIIA 10.4.6.2 Long residual effects

Not required as not triggered.

IIIA 10.4.6.3 Disorienting effects on bees

Not required as not triggered.

IIIA 10.4.7 Tunnel testing to investigate effects of feeding on contaminated honey dew or flowers

Not required as not triggered.

IIIA 10.5 Effects on arthropods other than bees

IIIA 10.5.1 Effects on sensitive species using artificial substrates

All studies were performed with the active substance QRD 460 and so may be viewed as a worst case for the product QRD 452 containing 16.75% QRD 460. In order to accommodate an issue with the standard protocol where the type of formulation was not compatible with the method and following the guidelines, tests were conducted with the active substance rather than the product, QRD 452.

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Non-target Terrestrial Arthropods (IIA 8.8.1.1)					
aphid parasitoid *Aphidius rhopalosiphi*	Acute contact, 24hr	QRD 460 a.s.	LR_{50} >200.00 L a.s./ha ER_{50} > 200.00 L a.s./ha NOEC repro = 200.00 L a.s./ha	ESCORT	[redacted], 2010a
predatory mite, *Typhlodromus pyri*	Acute contact, 24hr	QRD 460 a.s.	LR_{50} >200.00 L a.s./ha ER_{50} > 200.00 L a.s./ha NOEC repro 200.00 L a.s./ha	ESCORT	[redacted], 2010b
predatory bug, *Orius laevigatus*	Acute contact, 24hr	QRD 460 a.s.	LR_{50} >200.00 L a.s./ha ER_{50} > 200.00 L a.s./ha NOEC repro = 200.00 L a.s./ha	ESCORT	[redacted], 2010c
plant dwelling insect, *Coccinella septempunctata L.*	Acute contact, 24hr	QRD 460 a.s.	LR_{50} >200.00 L a.s./ha ER_{50} > 200.00 L a.s./ha NOEC repro = 200.00 L a.s./ha	ESCORT	[redacted], 2010d

All test results demonstrate that an extremely high rate (200 L a.s./ha) gives no significant effect on any of the non-target arthropods tested. The use of 100% QRD 460 active substance with the specified application rate equates to a rate of 168.6 kg a,s/ha, which is greater than 100 times the proposed rate of 1.523 kg a.s./ha, and is the LR_{50} value used for risk assessment purposes.

It is normal procedure to conduct a Tier 1 risk assessment on non-target terrestrial arthropods according to ESCORT II by calculating a Hazard Quotient, in-field and off-field to determine whether a risk is concluded or not.

The calculation is as follows:

$$\text{In-field HQ} = \frac{\text{application rate in g/ha x multiple application factor (MAF)}}{LR_{50} \text{ in g/ha}}$$

This means for QRD 452 "in-field" where MAF =1 as QRD 452 volatilises too quickly to have any further effect from subsequent applications;

$$HQ = \frac{1523 \times 1}{168600} = 0.009$$

The resulting HQ is less than the trigger of 2 and hence no potential in-field risk to non-target arthropods is concluded.

Considering the off-field HQ =

$$\frac{\text{application rate in g/ha x MAF x (drift (90}^{th}\text{ percentile) /veg distribution factor) x correction factor}}{LR_{50} \text{ in g/ha}}$$

If it is assumed that the veg distribution factor and the correction factor are both 10 and hence cancel each other out, and where MAF =1 as QRD 452 volatilises too quickly to have any further effect from subsequent applications, the only factor is drift and for the field use (glasshouse use is not considered relevant to NTAs) the value to cover use on melons and cucumber, both low field crops (less that 50cm height), would be at its highest, 2.77 (Rautmann *et al*, 2001, Table 10) at 1m distance. This is a maximum value.

This means for QRD 452 "off-field"

$$HQ = \frac{1523 \times 1 \times (2.77/10) \times 10}{168600} = 0.025$$

The resulting HQ is less than the trigger of 2 and hence no potential off-field risk to non-target arthropods is concluded.

The results of all the tests performed on all four species show no effects at the highest limit dose. This is not surprising as the active substance in QRD 452 volatilises rapidly leaving little or no residues available for exposure of non-target organisms within hours from the leaf surfaces, and within 48 hours from soil or water and indeed is predicted to break down in air in less than 48 hours. This means that both in the glasshouse or field, no effects are expected from the use of QRD 452.

On this basis, any risk to non-target organisms will be short and transitory in nature and the tests performed, acute contact over 24 hours, cover the potential risk period and demonstrate no concern at highly exaggerated and unrealistic rates. Both in-field and off-field Hazard Quotients have been calculated and conclude that there is no concern.

As such, it is proposed that there is an acceptable risk to non-target arthropods from the plant protection use of QRD 452 and no further work is required.

IIIA 10.5.2 Effects on non-target terrestrial arthropods in extended laboratory tests

Not required as not triggered

IIIA 10.5.3 Effects on non-target terrestrial arthropods in semi-field tests

Not required as not triggered

IIIA 10.5.4 Field tests on arthropod species

Not required as not triggered

IIIA 10.6 Effects on earthworms and other soil non-target macro-organisms

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Earthworms (IIA 8.9)					
Eisenia fetida	Acute, 14 day	QRD 452 16.75% EC formulation	LC_{50} > 1000 mg test item/kg dry soil NOEC = 1000 mg test item/kg dry soil.	OECD 207	[redacted] 2011

One acute study has been performed on earthworms with QRD 452, shown above.

From Section 5 Environmental Fate, a degradation study has been performed in soil; IIA 7.2.1. From this it was concluded that the three test items α-terpinene, p-cymene and d-limonene present in QRD 460 and its plant protection product QRD 452 disappear rapidly from the soil by evaporation. The DT_{50} of all three test items was calculated to be < 24 hours. The DT_{90} which was actually also the DT_{100} was < 48 hours.

This study confirms the assumptions made based on the physical-chemical properties of Terpenoid blend (α-terpinene, ρ-cymene, d-limonene) QRD 460 and the fugacity models conclusions that the fate of QRD 460 in soil is of limited relevance as it volatilises and evaporates rapidly into the air compartment.

IIIA 10.6.1 Toxicity exposure ratios for earthworms, TERA and TER_{LT}

Due to the physical-chemical properties of Terpenoid blend (α-terpinene, ρ-cymene, d-limonene) QRD 460, the active components in QRD 452 and their rapid volatilisation and dissipation in air, it is not possible to calculate a meaningful PEC soil because the active substance disappears from the soil compartment so rapidly.

This is confirmed by the soil degradation study where the DT_{50} was calculated to be < 24 hours and the DT_{100} was <48 hours. This suggests that it is unlikely that earthworms in the soil will come into contact with QRD 452. It is possible that earthworms on the surface might conceivably come into contact with soil but in that event, the results of the acute earthworm 14 day study suggest that QRD 452 is not toxic to earthworms.

On this basis no TERs have been calculated and the risk of QRD452 to earthworms is deemed acceptable.

IIIA 10.6.2 Acute toxicity to earthworms

It is not possible to calculate a meaningful PEC soil because QRD 452 volatilises so rapidly in air and the results of the acute earthworm 14 day study suggest that QRD 452 is not toxic to earthworms. Therefore no acute risk to earthworms is envisaged.

IIIA 10.6.3 Sublethal effects on earthworms

It is not possible to calculate a meaningful PEC soil because QRD 452 volatilises so rapidly in air and the results of the acute earthworm 14 day study suggest that QRD 452 is not toxic to earthworms. Therefore, no sublethal effects to earthworms are envisaged.

IIIA 10.6.4 Field tests (effects on earthworms)

As a DT_{100} is proposed for QRD 452 of < 48 hours in soil and the product volatilises into air rapidly, no chronic studies or chronic risk assessment is triggered. No TER is required.

IIIA 10.6.5 Residue content of earthworms

As a DT_{100} is proposed for QRD 452 of < 48 hours in soil and the product volatilises into air rapidly, no residue content of earthworms is to be expected.

IIIA 10.6.6 Effects on other soil non-target macro-organisms

As a DT_{100} is proposed for QRD 452 of < 48 hours in soil and the product volatilises into air rapidly no effects on other soil non-target macro-organisms are to be expected.

IIIA 10.6.7 Effect on organic matter breakdown

As a DT_{100} is proposed for QRD 452 of < 48 hours in soil and the product volatilises into air rapidly, no effects on other organic matter breakdown are to be expected.

IIIA 10.7 Effects on soil microbial activity

IIIA 10.7.1 Laboratory test to investigate impact on soil microbial activity

No laboratory tests have been instigated because with a DT_{100} proposed for QRD 452 of < 48 hours in soil and the knowledge that the product volatilises into air rapidly, no effects on soil microbial activity are to be expected.

IIIA 10.7.2 Further laboratory, glasshouse of field testing to investigate impact on soil microbial activity

Not required.

IIIA 10.8 Effects on non-target plants

IIIA 10.8.1 Effects on non-target terrestrial plants

The mode of action of QRD 452 is as an insecticide which rapidly volatilises into the air and is not observed to have any significant interaction with plants. Combined with no effects observed in any of the efficacy trials indicate no effect on the quality of plants or plant products, it is not anticipated that application of QRD 452 will affect non-target plants.

IIIA 10.8.1.1 Seed germination

QRD 452 is intended as a foliar application when seeds have already germinated. Further, there are no residues anticipated so seed germination will not be affected.

IIIA 10.8.1.2 Vegetative vigour

The mode of action of QRD 452 is as an insecticide which rapidly volatilises into the air and is not observed to have any significant interaction with plants. Combined with observations in all of the efficacy trials (details provided in the Biological Assessment Dossier) which indicate no effect on the quality of plants or plant products, it is not anticipated that application of QRD 452 will affect vegetative vigour

IIIA 10.8.1.3 Seedling emergence

QRD 452 is intended as a foliar application against insect that are present on established plants. Further, there are no residues anticipated so seedling emergence is no expected to be affected.

IIIA 10.8.1.4 Terrestrial field testing

The mode of action of QRD 452 is as an insecticide which rapidly volatilises into the air and is not observed to have any significant interaction with plants. Combined with observations in all of the efficacy trials (details provided in the Biological Assessment Dossier) which indicate no effect on the quality of plants or plant products, it is not anticipated that application of QRD 452 will affect terrestrial plants.

IIIA 10.8.2 Effects on non-target aquatic plants

IIIA 10.8.2.1 Aquatic plant growth – *Lemna*

A DT_{100} is proposed for QRD 452 of < 48 hours in water and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless.

Therefore there is no significant acute risk to non-target aquatic plants to be expected.

IIIA 10.8.2.2 Aquatic field testing

Not required and not triggered.

IIIA 10.9 Effects on other non-target organisms (flora and fauna) believed to be at risk

As the active components in QRD 452 volatilises into air rapidly and as a DT_{100} is proposed for QRD 452 of < 48 hours in water, soil and via animal metabolism and residues in plants are sufficiently low to be undetectable after 48 hours, therefore no other non-target organisms (flora and fauna) are believed to be at risk

IIIA 10.9.1 Summary of available data from preliminary tests used to assess biological activity and dose range finding, which may provide information on other non-target species (flora and fauna)

During development, a large number of laboratory and small scale plot or greenhouse studies have been carried out with QRD 452 or and its predecessor products. These have been undertaken to determine factors such as efficacy of product, efficacy of individual components, mode of action, effect of beneficial and non-target insects etc. A small subset of these tests and trials done by Agraquest Inc. and was selected as representative data, and presented in the Biological Assessment Dossier. This data demonstrated that QRD 452 was an effective insecticide against a range of soft bodied insect pests.

Since 2007, more than 700 field trials in the US have shown that both QRD 400 and 452 (plant extract and mimic based) products control aphids, mites, thrips, whiteflies and other pests. Typically QRD was used at 10 l/ha product. QRD 452 has been available as an insecticide in the USA since early 2009.

Further details are provided in the Biological Assessment Dossier (MIII Section 7).

IIIA 10.9.2 A critical assessment as to the relevance of the preliminary test data to potential impact on non-target species

During development a large number of laboratory and small scale plot or greenhouse studies have been carried out with QRD 452 or and its predecessor products. These have been undertaken to determine factors such as efficacy of product, efficacy of individual components, mode of action, effect of beneficial and non-target insects etc. A small subset of these tests and trials done by Agraquest Inc. and was selected as representative data, and presented in the Biological Assessment Dossier. This data demonstrated that QRD 452 was an effective insecticide against a range of soft bodied insect pests.

Since 2007, more than 700 field trials in the US have shown that both QRD 400 and 452 (plant extract and mimic based) products control aphids, mites, thrips, whiteflies and other pests. Typically QRD was used at 10 l/ha product. QRD 452 has been available as an insecticide in the USA since early 2009.

These data indicated that QRD 452 does not have a significant impact on non-target insects and is a useful product for use in Integrated Pest Management Programmes (IPM).

Further details are provided in the Biological Assessment Dossier (MIII Section 7).

IIIA 10.10 Other/special studies

IIIA 10.10.1 Other/special studies – laboratory studies

Not triggered or required.

IIIA 10.10.2 Other/special studies – field studies

Not triggered or required.

IIIA 10.11 Summary and evaluation of points IIIA 9 and IIIA 10.1 to 10.10, together with a detailed and critical assessment of the data

This nature of terpenoid compounds is well known. Naturally occurring and released terpenoids dissipate rapidly and these compounds are used in foods and as flavourings and in household products, to give a nice smell, amongst other uses. As such, the environment is exposed to them from natural and human sourced products and this exposure has been occurring for a very long time and at substantially higher amounts than any plant protection use is likely to result in. Ecotoxicological concerns have never been raised. The results of the work and risk assessment conducted for QRD 452 confirm this position of no concern and no significant risk.

As the levels of the active substance Terpenoid blend (α-terpinene, ρ-cymene, d-limonene) QRD 460 found on plants after application of the product QRD 452 are expected to be minimal due to the rapid volatilisation of the actives, thus exposure of avian species to QRD 452 is not expected to be significant via the oral route or due to contact with treated foliage or fruits. Also due to its rapid volatilisation from water, significant exposure is unlikely to occur to avians from drinking treated water.

The only likely exposure could be from air and it is proposed that the active substance QRD 460 degrades in air completely in less than 48 hours. Longest predicted DT_{100} for p-cymene was predicted to be 46.4 hours in air, the other two terpenoid components much shorter and so this is also an unlikely route of significant exposure, especially with the main use being in glass houses.

In one acute study on the Northern Bobwhite Quail a lack of toxicity was demonstrated with the result of an LC_{50} > 2250 mg/kg. A simplistic comparison of the above LC_{50} with the $PEC_{greenhouse\ air.}$ = 0.043 mg/L calculated in the Environmental Fate section is difficult to conclude from as a bird inhalation study would be needed to give a more meaningful comparison. However a mammalian inhalation study has been performed on QRD 460 and gave the following result: acute inhalation LC_{50} of QRD 460 is greater than 5.30 mg/L in male and female albino rats. Clearly this gives more than a 120 fold safety factor and indicates that even with a very conservative overestimate of exposure PEC calculation, the risk to birds is not of concern.

It has been shown in Section 5 Environmental fate and Behaviour, (IIA 7.8.3), that the three test items, α-terpinene, p-cymene and d-limonene were volatilized from the natural water test system rapidly with DT_{50}s of 4.1, 3.0, and 11.2 hours and DT_{90}s of 13.7, 9.4 and 10.0 hours, respectively. This means that a DT_{100} could be proposed for QRD 460 and its product QRD 452 of < 48 hours. QRD 452 is not persistent.

This means that exposure of aquatic organisms to QRD 452 only occurs for a few hours, if at all, as the plant protection product rapidly volatilises into the air., Therefore, it is unlikely that any exposure will reliably occur and if it does, it could be more from natural sources (in the plants around the aquatic systems) rather than the QRD 452 plant protection use, and as such has never generated concern. It is not possible to come up with a realistic PEC in water because of the speed of removal from the aquatic system and hence TERs cannot be reliably estimated as the levels of the components in QRD 452 are too low.

In one acute flow through study on the Fathead minnow, a lack of toxicity was demonstrated with the result of an LC_{50} > 1.17 mg /L and a NOEC 1.17 mg /L, the highest limit tested. It should also be noted that experimentally, the

active components in QRD 452 are not particularly soluble in water and so this limits the highest concentration available for testing. For this reason, the real LC_{50} is likely to be considerably higher. It is concluded that there is no significant risk to fish species from the use of QRD 452 and that further investigation with studies or calculations of TERs are not required as they would add nothing more to this conclusion.

In one acute flow through study on *Daphnia magna*, low toxicity was demonstrated with the result of an EC_{50} > 1.04 mg/L and a NOEC = 0.132 mg/L.

A DT_{100} is proposed for QRD 452 of <48 hours in water demonstrating that QRD 452 is not persistent and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless.

It is concluded that there is no significant risk to *Daphnia* from the use of QRD 452 and that further investigation with studies or calculations of TERs are not required as they would add nothing more to this conclusion.

In one acute flow through study on the sediment dwelling aquatic insect species, *Chironomus riparius*, low toxicity was demonstrated with the result of a 48-hour EC_{50} = 0.86 mg/L and a 48-hour NOEC = 0.360 mg/L .

A DT_{100} is proposed for QRD 452 of <48 hours in water demonstrating that QRD 452 is not persistent and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless.

Clearly any exposure of aquatic insect species to QRD 452 will be brief and transient and not expected to last as long as the study test exposure length.

It is concluded that there is no significant risk to Midge larvae from the use of QRD 452 and that further investigation with studies or calculations of TERs are not required as they would add nothing more to this conclusion.

Study design was limited by the poor solubility of the test materials which further supports the position that the risk to aquatics would be acceptable. In conclusion, no risk to any aquatic species are to be expected.

The product QRD 452 volatilises into air rapidly and has a DT_{100} proposed for QRD 452 of <48 hours in water, soil and via animal metabolism and residues in plants are sufficiently low to be undetectable after 48 hours.

The acute studies on mammals do not suggest concerns for dermal contact and inhalation and dietary exposure is expected to be minimal as fully explained in the Section 4 Metabolism and Residue summary. Thus it can be concluded that exposure to terrestrial vertebrates will be minimal as QRD 452 volatilises to air rapidly but where it does occur via inhalation or direct contact, the toxicity of QRD 452 is sufficiently low to cause no concern and the risk is acceptable. Dietary exposure would be minimal and so requires no further consideration.

The acute risk to bees from contact is expressed as a Hazard Quotient calculated by the following formula: (single application rate in g/ha, LD_{50} in µg a.i./bee); Hazard Quotient Q_{HC} = application rate / LD_{50}

Table 10.11-1 Risk to honey bees from contact exposure to formulated product (QRD 452 and QRD 420) containing QRD 460 in tomatoes, peppers, melons and curcubits as Hazard Quotient Q_{HC}

Test Substance	Exposure route	Application rate (g a.s./ha)	Endpoint	Value (µg a.i./bee)	Q_{HC}
QRD 420	contact	1523	LD_{50}	>100	15.23
QRD 452	contact	1523	LD_{50}	>100	15.23

The resulting Hazard Quotients are both clearly below the trigger of 50 indicating low risk to honey bees after the use of QRD 452.

These results also support the assumption that risk to other arthropods and insects are low from the plant protection use of QRD 452.

Four species of Non-target arthropods were tested in acute studies. The risk to non-target organisms is expected to be short and transitory in nature from QRD 452 and the tests performed, acute contact over 24 hours, cover the potential risk period and demonstrate no concern.

As such, it is proposed that there is an acceptable risk to non-target arthropods from the plant protection use of QRD 452 and no further work is required.

One acute study has been performed on earthworms with QRD 452, giving the results of LC_{50} > 1000 mg test item/kg dry soil and a NOEC = 1000 mg test item/kg dry soil.

From Section 5 Environmental Fate, a degradation study has been performed in soil; IIA 7.2.1 From this it was concluded that the three test items α-terpinene, p-cymene and d-limonene present in QRD 460 and its plant protection product QRD 452 disappear rapidly from the soil by evaporation. The DT_{50} of all three test items was calculated to be <24 hours. The DT_{90} which was actually also the DT_{100} was <48 hours.

This study confirms the assumptions made based on the physical chemical properties of the terpenoid blend QRD 460 and the fugacity models conclusions that the fate of the terpenoid blend QRD 460 in soil is of limited relevance as it volatilises and evaporates rapidly into the air compartment.

Due to the physical chemical properties of the active components in QRD 452 and their rapid volatilisation and dissipation in air, it is not possible to calculate a meaningful PEC soil because the active substance disappears from the soil compartment so rapidly. This is confirmed by the soil degradation study where the DT_{50} was calculated to be <24 hours and the DT_{100} was <48 hours. This suggests that it is unlikely that earthworms in the soil will come into contact with QRD 452. It is possible that earthworms on the surface might conceivably come into contact with soil but in that event, the results of the acute earthworm 14-day study suggest that QRD 452 is not toxic to earthworms. On this basis no TERs have been calculated and the risk of QRD452 to earthworms is deemed acceptable.

Equally as a DT_{100} is proposed for QRD 452 of <48 hours in soil and the product volatilises into air rapidly, no effects on other soil non-target macro-organisms, organic matter break down, microbial activity, or any other soil fauna or flora are to be expected.

The mode of action of QRD 452 is as an insecticide which rapidly volatilises into the air and is not observed to have any significant interaction with plants. Combined with no observations in any of the efficacy trials indicate an effect on the quality of plants or plant products, it is not anticipated that application of QRD 452 will affect non-target plants.

A DT_{100} is proposed for QRD 452 of <48 hours in water and the product volatilises into air sufficiently rapidly to make estimation of a realistic PEC_{water} difficult and sufficiently small as to be meaningless. Therefore there is no significant acute risk to non-target aquatic plants to be expected.

As the active components in QRD 452 volatilises into air rapidly and as a DT_{100} is proposed for QRD 452 of <48 hours in water, soil and via animal metabolism and residues in plants are sufficiently low to be undetectable after 48 hours, therefore no other non-target organisms (flora and fauna) are believed to be at risk

In conclusion, the use of QRD 452 according to the GAP proposed will result in acceptable risk to all ecotoxicologically relevant species as it rapidly volatilises and degrade in the environment and exposure is minimised. Natural sources of the same terpenoids have raised no concern and it is likely that natural exposure will far out way any exposure from the QRD 452 plant protection use proposed.

On this basis, Annex I listing is supported and no further work is required.

The studies performed and their endpoints are summarised below:

Table 10.11-1 Summary of Ecotoxicological Test Endpoints

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Avian (IIA 8.1.1)					
Northern Bobwhite Quail	Acute oral, single dose	QRD 406 plant extract a.s.	LC_{50} > 2250 mg/kg	US EPA OPPTS Number 850.2100	[redacted] & [redacted], 2007
Fish (IIA 8.2.1.2)					
Fathead minnow (*Pimephales promelas*)	Acute , 96 hr flow-through	QRD 460 a.s.	LC_{50} > 1.17 mg /L. NOEC 1.17 mg/L.	OECD 203	[redacted], 2011a
Invertebrates (IIA 8.3.1.1)					
Daphnia magna	Acute, 24 hr and 48 hr flow-through	QRD 460 a.s.	24- and 48-hour EC_{50} > 1.04 mg/L. 48-hour NOEC = 0.132 mg/L.	OECD 202	[redacted], 2011b
Invertebrates (IIA 8.3.2.1)					
Daphnia magna	Chronic, 21-day, flow-through	QRD 460 a.s.	21-day EC_{50} reproduction = 0.308 mg/L LOEC = 0.173 mg/L. NOEC = 0.214 mg/L.	OECD 211	[redacted], 2011c
Sediment Dwellers (IIA 8.5.1)					
Midge larvae (*Chironomus riparius*)	Acute, 48 hr flow-through	QRD 460 a.s	48-hour EC_{50} = 0.86 mg/L 48-hour NOEC = 0.360 mg/L	OECD 202	[redacted], 2011d
Bees (IIA 8.7.2)					
01/ Honey Bee *Apis mellifera*	Acute contact, 48hr	QRD 420 a.s.+ canola oil	LD_{50} > 100 µg a.i./bee.	OECD 214	[redacted] & [redacted] 2009a
02/	Acute	QRD 452		OECD 214	[redacted] & [redacted]

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Honey Bee *Apis mellifera*	contact, 48hr	16.75% EC formulation	LD_{50} > 100 µg a.i./bee.		[redacted] 2009b
Non-target Terrestrial Arthropods (IIA 8.8.1.1)					
aphid parasitoid *Aphidius rhopalosiphi*	Acute contact, 24hr	QRD 460 a.s.	LR_{50} >200.00 L a.s./ha ER_{50} > 200.00 L a.s./ha NOEC repro = 200.00 L a.s./ha	ESCORT	[redacted], 2010a
predatory mite, *Typhlodromus pyri*	Acute contact, 24hr	QRD 460 a.s.	LR_{50} > 200.00 L a.s./ha ER_{50} > 200.00 L a.s./ha NOEC repro 200.00 L a.s./ha	ESCORT	[redacted], 2010b
predatory bug, *Orius laevigatus*	Acute contact, 24hr	QRD 460 a.s.	LR_{50} >200.00 L a.s./ha ER_{50} > 200.00 L a.s./ha NOEC repro = 200.00 L a.s./ha	ESCORT	[redacted], 2010c
plant dwelling insect, *Coccinella septempunctata L.*	Acute contact, 24hr	QRD 460 a.s.	LR_{50} >200.00 L a.s./ha ER_{50} > 200.00 L a.s./ha NOEC repro = 200.00 L a.s./ha	ESCORT	[redacted], 2010d
Earthworms (IIA 8.9)					
Eisenia fetida	Acute, 14 day	QRD 452 16.75% EC formulation	LC_{50} > 1000 mg test item/kg dry soil NOEC = 1000 mg test item/kg dry soil.	OECD 207	[redacted] 2011

IIIA 10.11.1 Predicted distribution and fate in the environment and the time courses involved

QRD 452 volatilises and degrades in < 48 hours. On this basis, its distribution and fate are not relevant as it rapidly moves from the soil and water compartments of the environment to the air and then rapidly dissipates and breaks down. It is not persistent.

This nature of terpenoid compounds is well known. Naturally occurring and released terpenoids dissipate rapidly and these compounds are used in foods and as flavourings and in household products, to give a nice smell, amongst other uses. As such, the environment is exposed to them from natural and man-made products and this exposure has

been occurring for a very long time and at substantially higher amounts than any plant protection use is likely to result in. Ecotoxicological concerns have never been raised.

IIIA 10.11.2 Non-target species at risk and extent of potential exposure

None are considered at risk due to the short life of QRD 452 in the environment.

IIIA 10.11.3 Short and long term risks for non-target species, populations, communities and processes

None are considered significant due to the short life of QRD 452 in the environment.

IIIA 10.11.4 Risk of fish kills and fatalities in large vertebrates or terrestrial predators

None are considered likely due to the short life of QRD 452 in the environment.

IIIA 10.11.5 Precautions necessary to avoid or minimize contamination of the environment and for the protection of non-target species

None are considered necessary due to the short life of QRD 452 in the environment.