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IIIA 10ECOTOXICOLOGICAL 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 inbrospides* near *ambrosioides* for use as an insecticide plant protection product. The product is Requiem C (QRD 452) an emulsifiable concentrate which is foliar applied to control compon insect pests of protected and open field open. It contain 16.75 % (w/w) of the active substance: Terpenoid blend (α -terpinene -cymene, d-lanonene) QRD 460.

To defend themselves against herbivores and pathogena plants naturally release a variety of volatiles including various alcohols, terpenes and aromatic compounds. These volatiles can defer insects or other herbivores from feeding, can have direct toxic effects on pests, or they may be involved in recruising products, and parasitoids in response to feeding damage (*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 a terpinene, programmed and d-limonene, have been identified as candidates for biopesticidal activity as this naturally occurring combination is the key active moiety, they are considered and to me to be on 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 prowing 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 HU with ctgb betherlands as the Rapporteur Member State. It is an insecticide for use on domatoes and peppers in glasshouses and cucurbits in glasshouses and field at a maximum application rate of 1.523 kg a.s./has to 3 junes with a 7 day interval between treatments.

	Queta		Application	🏷 Max. App	olication	Minimum
Region	Proteeted (Applications	> Interval	Rate	Water	PHI
Å			(days)	(kg as/ha)	(L/ha)	(days)
N EU	Protected	3 4		0.381 - 1.523	400 - 1000	0
S EV	Protected	Q ~3 L		0.381 - 1.523	400 - 1000	0
S[*]E U	Ofutdoor	°~°3	7	0.762 - 1.523	400 - 1000	0
7	. Or	Čí 😵				

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

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 msect 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 noteworth that these terpenes, α -terpinene, p-cymene, and d-limonene, are commonly used as fragrances and flavourings coint 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, tomato s celery and carrots, with various functions as secondary metabolites (**1990**). 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 factor 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 behavior 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 any 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 ogen from the other man@natural sourceOf the three to the the other man@natural sourceOf the three to the the other man@natural sourceOf the three to the the three to the three to the three to the three to the the constituents of QRD 452, a-terpinene, p-cymene, d-limonene. They are present in abundance in many here plants, and are common in many other edible plants such as oftrus fruits, tomatoes, celery and carrots, with various ,. et al, (2016). Consequent othey form a significant part of both human functions as secondary metabolites (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 day concern. The three terpened 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 EV registered ot pending active substances: tea tree oil, thyme oil, orange oil citronetta, spearmint of, tagetes (margold) of n

As a result of their nature, it was not possible recalculate 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 PERs of ETEs is there is no meaningful dietary exposure and no figure for concentration in the diet from use of QRD 45 exceptizero.

Tests were performed on the QRD 52 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 siny conference. The results of the studies generally demonstrate that no effects were seen whe light 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 to concern with respect to risk a 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

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

QRD 406 - Chenopodium ambrosioides near ambrosioides plant extract technical grade active ingredient (tgai) consisting of the three terpettes 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 is FACIN 25K in some reports and registered in the USA as Requiem[®] 25EC and Metronome™.) The three teppenes QRD #00 comprise approximately 17%.

QRD $\frac{1}{20}$ = blowed to the state three terpenes in the same concentrations as found in QRD 406 with plant derived impubilies replaced with carola oil. The three terpenes comprise approximately 67% of QRD 420.

QRD 406 = 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.

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ORD 452 = ORD 416 - due to a code designation error, the product was re-coded as ORD 452. There are a fewstudies that reference ORD 416, but the composition is identical to ORD 452. (Also known and registered in the USA as Requiem[®] EC and Metronome[™] EC). The concentration of the three terpenes in ORD 416 and ORD 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 impundities. 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 ORD 400 are the same.

IIIA 10.1 Effects on birds

IIIA 10.1	Effects on k	oirds
IIIA 10.1.1	Acute toxici	ty exposure ratio (TERA) for birds
Species	Test type	Test substance (a.s. or formulation)
Avian (IIA 8.1.	1)	
Northern Bobwhite Quail	Acute oral, single dose	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

Estimated Theoretical Exposure calculations are usually based of dietary exposure of brids 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 othe concentration in food, as anything other than zero. Coupled with the predominant glasshouse use, it is more likely that any exposure could be from ratural cources rather than QRD 452. Therefore an ETE and hence TOR cannot be reliably stimated.

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

The only likely exposure ould be from air and it is proposed that the QRD 460 degrades in air completely in less than 48 hours doingest predicted DT₁₀₀ for p-Qmene was predicted to be 46.4 hours in air, the other two terpene components, much shorter) and so this is also an unlikely rate of significant exposure, especially with the main use en alter being in glass houses.

In one acute study on the Northern Bodwhite Quail, a Pack of toxicity was demonstrated with the result of an LC50> 2250 mg/kg. Mammahan studies from the Toxicology section also suggest a low level of toxicity to other species.

A simplistic comparison of the above Leso with the PEC greenhouse air. = 0.043 mg/L calculated in the Environmental Fate section is difficult to cover lude from as a bird inhalation study would be needed to give a more meaningful comparison, Rowever a maximalian inhalation study has been performed on QRD 460 and gave the following result: acute inhalation LCG of QRD 460 is greater than 5.30 mg/L in male and female albino rats. Clearly this gives more that a 120 fold safety factor and indicates that even with a very conservative overestimate of exposure PEC calculation, the rsk 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 of 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 (TERst) 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 is 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.

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

QRD 452 is not applied as a bait.

- In the case of pellets, granules prills or treated seed **IIIA 10.1.4**
- Amount of the active substance in or on each pellet, granule, pril or treated seed IIIA 10.1.4.1

QRD 452 is not applied as a pellet, granule, prittor as a seed areatment.

and per gram of Proportion of the LDs for the active substan IIIA 10.1.4.2 particles

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

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

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

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

QRD 452 is not applied as a petter, gramile, prill or as a

Supervised cage or field thats IIIA 10.1.7 Ó QRD 452 is not applied as a petter, granule, part or as a seed treatment.

Acceptance of bait, grantiles or treated seeds by birds (palatability test) **IIIA 10.1.8** 0

QRD 452 is not applied as a failet, granule, and or as a see greatment.

Effects of secondary poisoning IIIA 10 9.9

QRD 52 is not applied as a pellet, granule, prill or a seed treatment.



Effects on aquatic organisms

AgraQuest, Inc.	Requiem [®] EC (QRD 452)	Doc M III, Sec. 6
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Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Fish (IIA 8.2.1.2)			~	
Fathead minnow	Acute, 96 hr	QRD 460		OEOD 203	2011a
(Pimephales promelas)	flow-through	a.s.	$LC_{50} > 1.17 \text{ mg}/L$		
_ , _			NOEC1.17 mg /L.		

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, p-cymene, and d-limonene were volatilized from the natural water test system rapidly with DT₅₀Sof 4.14 3.0, and 11.2 hours and DT₉₀s of 13.7, 37.4 and 10.0 hours for α -terpinene, p-cymerie, and e-limonene, respectively. This means that a DT₁₀₀ could be proposed for QRD 460 and its product QRD 452 of C48 hours QRD 452 is not persistent.

 \bigcirc

This means that exposure of aquatic organisms to QRD 452 only occurs for a matter of hours of at all, as the plant protection product rapidly volatilises into the arr. It is unlikely that any exposure will reliable occur and if it does, it could be more from natural sources in the plants around the agratic softems of the data 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 THRS cannot be reliably Stimated as the levels of the components in QRD 452 are to yow.

In one acute flow through study on the Fathead mannow a lack of toxicity was demonstrated with the result of an $LC_{50} > 1.17 \text{ mg}/L$ and a NOEC 17 mg/L, the highes Gimit tested. It should also be noted that experimentally, the active components in QRD 452 are not particularly soluble in water and so this finits the highest concentration available for testing. For this reason, the real LC_{50} is likely 0 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 converted that there is no significant risk to aquatic species from the use of QRD 452 and that further investigation with stories of calculations. 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 TA TERA for fish

A DT₄₀₀ 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 $_{abc}$ difficult and afficiently small as to be meaningless.

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

IIIA 10.2.1,2 TERLT for fish

As a DK_{00} 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*

AgraQuest, Inc.	Requiem [®] EC (QRD 452)	Doc M III, Sec. 6
June 2011	Terpenoid blend (a-terpinene, p-cymene, d-limonene) QRD 460	Page: 11 of 28

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Invertebrates (II	(A 8.3.1.1)			*	N O
Daphnia magna	Acute, 24 hr and 48 hr flow-through	QRD 460 a.s.	24- and 48-hour EC ₅₀ > 1.04 mg/L.	OFOD 202	
			NOEC = 0.132 mgP .		

In one acute flow through study on Daphnia magna, low toxicity was demonstrated with the result of an EC mg/L and a NOEC = 0.132 mg/L.

A DT100 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 PPC difficult and sofficiently 1 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 B'sufficiently low and of no real concern.

It is concluded that there is no significant risk to Daphinia 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.

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

IIIA 10.2.1.4 TER_{LT} for Daphria

<48 bours in water and the product volatilises into air rapidly, no chronic As a DT₁₀₀ is proposed for QRD 452 0 studies or chronic risk assessment is triggered and therefore for TER is required. Ô

n

IIIA 10,2,1.5	TERA for an	aquatic insect s	pecies 2		
**	<u> </u>				
Species	Test type 🌱	Fest 🔊	Toxicological Endpoint	Test	Ref
	¢ A	Substance 🔍			
a		(a.s. or	Ô ^y Ô ^y	Guideline	
~Q	Û, Û	formulation)			
. () . ()	Ő,				
Sediment Dwelle	rs (IIA & 5.1) 🦼				
Midge larvae	Acute, 48 hr	QRD 460	, ~ Q *	OECD 202	, 2011d
(Chironomus	flow-throagh		C ⁷		f
riparius)	, Or	a.s.	48-hour EC ₅₀ = 0.86 mg/L		
-					
Å	A X		48-hour NOEC = 0.360		
			mg/L		
Â. Î		S Y	<u> </u>		
		*	l	1	

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

A DT165 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 PECwater 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 fevel of toxicity to other species), suggest that additional work is unnecessary as the toxicity is sufficiently low and of poreal 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 TSR 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 equired

IIIA 10.2.1.7 TERA for an aquatic crustaceany species

A DT₁₀₀ 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 meaningly so.

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

IIIA 10.2.1.8 TERLT for an aquatic crostacean species

As a DT₁₀₀ is proposed for ORD 452 of <48 hours in water and the product votatilises that air rapidly, no chronic studies or chronic risk assessment is triggered. NO TER or required.

IIIA 10.2.1.9 TERA for an aquatic gastropod mothisc species

A DT₁₀₀ 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 smalles to be meaningless.

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

IIIA 10.2.1.10 TEBLT for an aquatic gastropod mollasc species

As a DT_{100} is proposed to QRD 52 of 48 hours in water and the product volatilises into air rapidly, no chronic studies or chrome risk assessment is traggered. No TER is required.

IIIA 10.2 111 TERLT for algae

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

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 LC₅₀/EC₅₀

This is not an EC data requirement.

IIIA 10.2.2.5 Marine sediment invertebrates, acute toxicity LC₅₀

This is not an EC data requirement.

IIIA 10.2.3 Microcosm or mesocosm study

, no microcosm integur rapidly, atilises As a DT₁₀₀ is proposed for QRD 452 of <48 hours in water and or mesocosm studies are triggered.

IIIA 10.2.4 Residue data in fish (long-term)

votatilises are apidly and breaks As a DT100 is proposed for QRD 452 of 48 hours in wher and he product down rapidly, no chronic studies or chronic risk assessment is triggered.

Chronic fish foxicity data **IIIA 10.2.5**

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

a, As a DT100 is proposed for QRD 452 of 48 hours in wher and the product valatilises into air rapidly, no chronic studies or chronic risk assessment is triggered L

Fish early life stage toxicity test IIIA 10.2.5.2

48 hours in water and the product waterlises into air rapidly, no chronic As a DT₁₀₀ is proposed for QRD 452 of studies or cheonic risk assessment is friggered. No FER is required,

IIIA 10.2.5.3 Fish life cycle tes

À



IIIA 10.2.6 Chronic toxicity to aquatic invertebrates

IIIA 10.2.6.1	Chronic toxicity	v in <i>Dat</i>	ohnia magn	<i>a</i> (21-dav)
1111 100-0001		, <i>–</i> p		

Species	Test type	Test substance (a.s. or formulation)	Toxicological Endpoint	Test Guideline	Ref
Invertebrates (II	A 8.3.2.1)			<i>a</i>	4
Daphnia magna	Chronic, 21- day, flow- through	QRD 460 a.s.	EC ₅₀ reproduction = 0.308 mg/L LOEC 0.173 mg/L.	OECD 211	

In one chronic flow through study on *Daphnid hagna*, flow to city was demonstrated with the result of an \mathcal{C}_{50} for reproduction = 0.308 mg/Land a NOEC = 0.214 mg/L.

A DT₁₀₀ is proposed for QRD 452 of **F8** hours in water definition of a readistic PEC water deficiently 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 in ufficiently low and other endoncement.

It is concluded that there is no significant acute or chronic risk to Daphyla 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 iono significant chronio isk to aquatic species and no TER is required.

IIIA 10.2.6.2 Chronic toxicity for a pepresentative species of aquatic insects

As a DT_{10} 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 by greed. No TER is required.

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

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

IIIA 40.2.7 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 line 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.

AgraQuest, Inc.	Requiem [®] EC (QRD 452)	Doc M III, Sec. 6
June 2011	Terpenoid blend (α-terpinene, ρ-cymene, d-limonene) QRD 460	Page: 15 of 28

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 D_{50} of QRD $\oplus 60$ is greater than 5050 mg/kg in male and female rats thus demonstrating a lack of toxicity at the highest limit dose and hus any risk from application of diluted QRD 452 would be even less.

A simplistic comparison of the acute inhalation LC_{50} of QCD 460 > 5.30 kmg/L in male and female albino rats MA 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 REC 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 that for QRD 460, published data exist for its terpene components pcymene 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 a terpinene will be metabolized in essentially the same manner as pcymene and d-limonene. Following of oral dose, the components of QRD 460 are tapidly 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 dosorbed via the oral route is similar in different species; reported values range from 50-96% in rats, guinea-pies, hamsters and dogs whilst those in human male volunteers are reported as 50-80% (Koduma *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 pcymene (70-80%) in rats and guinea pigs with recover 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 exercise 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 toricity of QRD 452 is sufficiently low to cause no concern and the risk is acceptable. Dictary exposure would be minimal as fully explained in the Section 4 Metabolism and Residue summary and so requires no further consideration.

\$1

IIIA 10.3.1.2 Short term toxicity exposure ratio (TERst)

The product QRD 452 votabilises into air apidly and as a DT₁₀ s proposed for QRD 452 of < 48 hours in water, soil and via animal methodism and residues in plants are sufficiently low to be undetectable after 48 hours therefore no further short term studies coshort tick assessment is triggered. No TER is required.

IIIA 10.301.3 Long-term toxicity exposure ratio (TER_{LT})

The product QRD 452 volations in Gair 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 studie for chronic risk assessment is orgagered. 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

Acceptance of bait, granules or treated seeds by terrestrial vertebrates (palatability IIIA 10.3.2.2 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 C Toxicological Entepoint Test Ref
		(a.S. or formulation)
	~	
Bees (IIA 8.7.2)	×.	
01/	Acute 🔊	QRD 420 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
	contact, 48hr	
Honey Bee Apis	Č Ő	$a.s. \pm canola$ LD $_{50} > 100 \mu g a.i. Bee. \leq 100 \mu g$
mellifera	Q' L.	
02/	Acute	QRD 452 (10) 20 (10) 00 (10) (10)
	condact, 48hr	2009b
Honey Bee Apis	×.	46.75% EC $PLD_{50} > 100 \mu G a.i./bee.$
mellifera		formulation of the original of
**		
	¢ A	
	~~ ~~	

Two studies or been performed, one on an older formulation QRD 420 and one on the current formulation submitted for registration here, QRI0452.

Oral exposure Qno. ш A 10¥.1.1

As the potential for oral monosure similar as RD 452 volatilizes into air leaving no measurable residues on crops or potential we foodstuffs such as poller within a very short time (less than 48 hours) it was not considered via the oral pathway. necessary to test the

Contact exposure Q_{HC} Ш

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 Ouotient calculated by the following formula: (single application rate in g/ha, LD₅₀ in µg a.i./bee)

Hazard Quotient Q_{HC} = application rate / LD₅₀

Table 10.4.1.2-1 Risk to honey bees from contact exposure to formulated product (ORD 452 and ORD containing QRD 460 in tomatoes, peppers, melons and curcubits as Hazard Quotient QHC

Test Substance	Exposure route	Application	Endpoint	Value	Que C
		rate (g a.s./ha)	ĈĄ	(pig a.i./bee)	
QRD 420	contact	1523	TLD50		
QRD 452	contact	1523	LD ₅₀		۲۶.23 م م

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

Acute toxicity of the preparation to **IIIA 10.4.2**

IIIA 10.4.2.1 Acute oral toxici

Please see 10.4.1

IIIA 10.4.2.2 Acute contact

Please see 10.4.1

C AND O

Investigation of special offects

IIIA 10.4.6.1

Not required as not triggered

Long residual effects **IIIA 10**

Not required a pot triggered. IIIA 10.46.3 **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 use with the sondard 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.

	r				
Species	Test type	Test	Toxicological Endpoint	Test 🗸	Rei
		substance		Ŷ Ò`	
		(a.s. or		Guideline	4
		formulation)		·0 ~	
				Å.	
Non-target Terr	estrial Arthrop	ods (IIA 8,8.1.1)			
aphid parasitoid	Acute	QRD 460 🖉	LR >200,00 Las ha 🗘	ESCORT 0	, 2010a
Aphidius	contact, 24hr	2 6		D D	22
rhonalosinhi		a.s.	$ER_{50} > 200.00 L a.s./ha$		°~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
		0, 5			
	~		NOEC repro= 20000 L	o o	<i>v</i>
	×.	(& .C ^y	as /ha		
	, Q	O' N			
predatory mite	Acute	AQRD 460 🖉	LR5@> 200,60 L a.s./ha	ESCORT	. 2010b
Typhlodromus	contact, 24hr			\sim	, _ · · · · ·
nvri		a.s.Q	$ER_{50} > 200.00 L a.s./ha^{\circ}$	s,	
Pyrv		<u>, 9</u> , 7			
	õ .v		NOEC repro200.00		
		`~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	a. Sha 🐎		
Ŭ.					
predatory bug,	Acute 🔬	QRD 460 (LR50 >200.0 @L a.s./hor	ESCORT	, 2010c
Orius S	contac Q24hr	F & .			
laevigatus		a.s. S	$ER_{50} > 200.00 L_{x}^{3} a/s./ha$		
0	\$° 4'				
	6 A		NOEC repro 200.00 L		
			a.s. a		
~0		N N			
plant dwelling	Acute	QRD 4662	2R ₅₀ 200.00 L a.s./ha	ESCORT	, 2010d
insect,	contact, 24hr	d o s	× " ~		
Coccinetta		va.s	ER > 200.00 L a.s./ha		
septempunctata	X A				
L.		X Q	NOEC repro = 200.00 L		
6			a.s./ha		
_4					
<u>()</u> "		••• @			

All test results demonstrate that an extremely high rate (200 L a.s./ha) gives no significant effect on any of the nontarget arthropods ested. 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 LR₅₀ 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.

AgraQuest, Inc.	Requiem [®] EC (QRD 452)	Doc M III, Sec. 6
June 2011	Terpenoid blend (α-terpinene, ρ-cymene, d-limonene) QRD 460	Page: 19 of 28

The calculation is as follows:

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

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

> $1523 \ge 1 = 0.009$ HO =

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

Considering the off-field HQ =

application rate in g/ha x MAF x (drift (90th percentile) /veg LR50 in g/ha

If it is assumed that the veg distribution factor and the correction factor are both 10 and hence canceleach 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 (glosshouse use is not considered relevant to NTAS) the value to over use on melons and cucumber, both low field cops (less that 50cm height), would be at its highest 77 (Reautmann et al. 2001, Table 10) at 1m distance. This is a maximum value.

This means for ORD 452 "off-field"

$$HQ = \frac{1523 \times 100}{2168600} \times 10^{0} = 0.025$$

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 45% 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 tess than 48 hours. This means that both in the glasshouse or field, no effects are expected from the use of QRD 45.

On this basis, any rise to non-target organises will be short and transitory in nature and the tests performed, acute contact over 24 hours, cover the potential risk period and depronstrate 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.

won-target arthropods from the plant protection use of QRD As such, it is proposed that there 452 and a further work is required

target terpestrial arthropods in extended laboratory tests **IIIA 10.5.2** £itects on non

Not required

on gon-target terrestrial arthropods in semi-field tests not toggered

IIIA 10.5.4 Field tests on arthropod species

AgraQuest, Inc.	Requiem [®] EC (QRD 452)	Doc M III, Sec. 6
June 2011	Terpenoid blend (α-terpinene, ρ-cymene, d-limonene) QRD 460	Page: 20 of 28

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 Gutteline	Ref A A
Earthworms (IIA	A 8.9)		à.	*	
Eisenia fetida	Acute, 14 day	QRD 452 16.75% EC formulation	$LC_{50} > 1000 \text{ mg test item/kg}$ dry soil NOEC = 1000 mg test item/kg dry soil.	OECD 20	

One acute study has been performed on earthworms with QRD 4\$2, shown above.

From Section 5 Environmental Fate, a degradation study has been performed in soil. IIA 7.2.1. From this fewas concluded that the three test items α -terpinone, p symene and d-limonene present in QRD 460 and its plant protection product QRD 452 disappear rapidly from the Seil by Staporation. The DT₅₆ of all three test items was calculated to be < 24 hours. The DT₅₀ which was actually also the DT₁₀ was 48 hours.

This study confirms the assumption made based off the physical chemical properties of Serpeneid 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 satios for eacthwords, TERA and TERLT

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

This is confirmed by the soil degradation study where the DT_{50} was calculated to be < 24 hours and the DT₁₀₀ 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 earthworm on the pirface might conceived y come into contact with soil but in that event, the results of the acute earthworm 14 day study suggest that QRD 452 is not tox of to earthworms.

On this basis no TERs have been calculated and the risk of QRD 2 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 arthworm 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 $\sqrt[3]{2}$ 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 volatives into air rapidly, no effects on other soil non-target macro-organisms are to be expected.

IIIA 10.6.7 Effect on organic matter break fown

As a DT₁₀₀ is proposed for QRD 452 of < 48 hours in soil and the product voltatilises into an rapidly no effects on other organic matter breakdown are to be expected $\sqrt{2}$

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 DT₁₀₀ proposed for ORD 452 of 48 hours in soil and the knowledge that the product volatilises into an rapidly, no affects of soil merobia 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 Effectson non-target plants

IIIA 10.8.1 > Effects on Pon-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 nontarget 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 45278 as an insection 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 bossies) which indicate no effect on the quality of plants or plant products, it is not anticipate that application of QRD 452 will affect vegetative vigour

IIIA 19.8.1.3 Sections emergence

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

Terrestrial field testing IIIA 10.8.1.4

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 of 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

o air Suffictently rapidly to A DT_{100} is proposed for QRD 452 of < 48 hours in water and the product volatilises into air A DT₁₀₀ is proposed for QKD 432 OI \sim 40 nours in which and sufficiently small as to $\frac{1}{\sqrt{2}}$ meaningless

Therefore there is no significant acute risk to non-target adjuatic plants to be

IIIA 10.8.2.2 Aquatic field testing

Not required and not triggered.

fanna) believed to be and **IIIA 10.9** Effects on other non at risk

As the active components in QRD 452 volatifises into air repidly 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 (Nora and fauna) are believed to be at cisk

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

During development, a large number of aboratory and small scale plot or greenhouse studies have been carried out with QRD 452 of 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 sected as representative data, and presented in the Biological Assessment Dessier. This data demonstrated that QRD 452 mas an effective insecticide against a range of soft bodied insect pests?

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

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

A critical assessment as to the relevance of the preliminary test data to IIIA 40.9.2 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 45% or and its prefeccessor, products. These have been undertaken to determine factors such as efficacy of product, efficacy & 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.

AgraQuest, Inc.	Requiem [®] EC (QRD 452)	Doc M III, Sec. 6
June 2011	Terpenoid blend (α-terpinene, ρ-cymene, d-limonene) QRD 460	Page: 23 of 28

These data indicated that ORD 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**

Ô

Not triggered or required.

IIIA 10.10.2 Other/special studies – field studie

Not triggered or required.

d HEA 10-1 to 10 + ----Summary and evaluation of points LIA 9 and LIA 10-1 to 10.10 **IIIA 10.11** together with a detailed and critical assessment of the data

This nature of terpenoid compounds is well thown Naturally occurring and released terpenoids dissipate rapidly and these compounds are used in foods and as flavourings and in household products, to give a meet small, amongst other uses. As such, the environment is exposed to them from natural and human sources products and this exposure has been occurring for a very long time and at substantially higher amounts than any plant protection ase 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 Terpenord blend (a-terpinene, p-cymene, d-famonene) QRD 460 found on plants after application of the produce 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 rand volatifisation from water, significant exposure is unlikely to occur to avians from prinking 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 the hours (longest predicted DI to for p-cymethe was predicted to be 46.4 hours in air, the other two terpenoid components, much shorter) and so this is also an Onlikely route of significant exposure, especially with the main use being inglass houses

In one acute study on the Northen Bobwhite Quail, a lack of toxicity was demonstrated with the result of an LC50> 2250 mg/kg. A simplify comparison of the bove LC_{50} with the PEC greenhouse air. = 0.043 mg/L calculated in the Environmental Fate section is difficult to conclude from an 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 i@halatim LC50 @QRD@60 is @eater 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 to not obconcered.

It has been shown in Section 5 Environmental tate and Behaviour, (IIA 7.8.3), that the three test items, α-terpinene, p-cyntene and d-limeopene were volatilized from the natural water test system rapidly with DT50s of 4.1, 3.0, and 11.2 hours and DT₂₀s of 1027, 37 and 10.0 hours, respectively. This means that a DT₁₀₀ 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 product product product product product and the air., Therefore, it is unlikely that any exposure will reliably occur and if it does a could be more from atural 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 peed 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

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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 $E_{50} > 10^4$ 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 perficiently 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 *ChironomyOriparites*, low exicity was demonstrated with the result of a 48-hour $EC_{50} = 0.86 \text{ mg/L}$ and 48-hour NOEC = 0.86 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 Secies to QRD 452 will be brief and transient and perfected to last as long as the study test exposure length

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

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

The product QRD 452 volations into air rapidly and has $a \Phi T_{100}$ proposed for QRD 452 of <48 hours in water, soil and via animal metabolism and residues in plants are sufficiently low to be underscale 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 Merabolism 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 poxicity of QRD 452 is sufficiently low to cause no concern and the risk is acceptable. Distary exposure would be minimal and exrequires no further consideration.

The acute risk to bees from contact is expressed as Hazard Quotient calculated by the following formula: (single application rate in g/ha UD_{50} in ug 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 comatoes, peppers, metons and curcubits as Hazard Quotient Q_{HC}

Test Substance Exposure route	Application rate (g st.s./ha)	Endpoint	Value (µg a.i./bee)	Q _{HC}
	ş q			
QRD 420 contact	@1523	LD_{50}	>100	15.23
	₽Ŷ			
QRD 492 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 QED 452, giving the results of LC_{50} 1000 60 g test 0 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-cyfnene and d-timonene present in QDD 460 and it plant protection product QRD 452 disappear rapidly from the soil-by evaluation. The DT₅₀ of all three test items was calculated to be <24 hours. The DT₉₀ which was actually also the DT₁₀₀ was <48 hours.

This study confirms the assumptions made based on the physical chemical properties of the terpenoid blefa QRD 460 and the fugacity models conclusions that the fate of the terpenoid blend QRD 460 in soil is of limited belevance 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 sind volatilisation and dissipation in air, it is not possible to calculate a maningfit DPEC soil because the active substance disappears from the soil compartment so rapidly. This is confirmed by the soil degradation study where the DT₅ was calculated to be <24 hours and the DT₁₀₀ was solver. This acgregests that it is unlikely that earthworms in the soil will come into contact with QRD 452. It is possible that earthworms on the curface 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 hot toxic to earthworms. On this basis no TERs have been executed and the risk (QRD 52 to earthworms is deemed acceptable.

Equally as a DT₁₀₀ is proposed for QRD 452 of <45 hours in soil and the product volatilises into air rapidly, no effects on other soil and the product volatilises into air rapidly, no any other soil fauna or flora are to be expected.

The mode of action of RD 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 quanty of plants of plants of plants of plants of the efficacy trials indicate an effect of the application of QRD 452 will affect non-target plants.

A DT₁₀₀ is proposed for QRD 452 of <48 hours in water and the product volatilises into air sufficiently rapidly to make estimation of a respect of the product volatilises into air sufficiently rapidly to significant acute risk to non-target aquaric plans to be expected.

As the active components in QRD 452 volatilises into an rapidly and as a DT_{100} is proposed for QRD 452 of <48 hours in water, soil and vola 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, Andrex I listing is Supported and no further work is required.

The studies performed and heir endpoints are summarised below:

 Table 10.11-1
 Summary of Ecotoxicological Test Endpoints

Species	Test type	Test substance	Toxicological Endpoint	Test Guideline	Ref	
		(a.s. or formulation)				
Avian (IIA 8.1.1	.)			ð		
Northern Bobwhite Quail	Acute oral, single dose	QRD 406		OPPTS	\$ 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	
Doowinte Quan	C	plant extract a.s.	LC ₅₀ > 2250 mg/kg	Number >>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>		
			<u> </u>			
Fish (IIA 8.2.1.2))					
Fathead	Acute, 96 hr	QRD 460		O₽¢D 206 ⁹	, 20 11a	
minnow	~			Ø D		
(Pimephales	flow-through	a.s.	$\mathcal{L}_{50} > 1.1^{\circ} / \text{mg/l}^{\circ}$			
promelas)		A.	* NOE 1.17 mg /L.			
Invertebrates (II	A 8.3.1.1)				y O	
Daphnia magna	Acute, 24 hr and 48 hr	QRD 460	24-xand 48-hour	OFCD 202	,	
	flow-through	a.s. S	$F_{50} > 104 \text{ mgA}.$		29110	
	×	× , 8	48-hours		2	
			NOTEC = 0^{132} mg/L.			
Invertebrates (II	A 8.3 2.1)			4 [']		
Daphnia magna	Chronic 21- Clay, flow- through	QR1D 460 , ⁹ ~	\mathbf{EO}_{50} reproduction = 0.308	OECD 211	, 2011c	
٥ پ		P A 1	g mg/D			
			OEC 0.173 mg/L.			
	3		NOPC = 0.214 mg/L.			
Sediment Dwelle	Sediment Dwellers (IIAS 5.1)					
Midge larvae	Acute, 48 b	QRD 460	à à	OECD 202	 ,	
(Chironomus riparius)	flow-through	a.s.	48 bour EC ₅₀ = 0.86 mg/L		2011d	
	S A		48-hour NOEC = 0.360			
			mg/L			
Bees (IIA 8.7.5)						
01/	Acute C	QRD 420		OECD 214	&	
Honey Bee App		a.s.+ canola	$LD_{50} > 100 \ \mu g \ a.i./bee.$		2009a	
mellifera		oil				
02/	Acute	QRD 452		OECD 214	&	

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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.	No.	
Non-target Terro	estrial Arthrop	ods (IIA 8.8.1.1)	د به لا به	↓ <u>`</u>	
aphid parasitoid Aphidius rhopalosiphi	Acute contact, 24hr	QRD 460 a.s.	LR ₅₀ >20000 L a.s./ha	ESCORT	2010
		(NOTEC repro = 200.00 L		
predatory mite, <i>Typhlodromus</i> <i>pyri</i>	Acute contact, 24hr	QRD 460	LR ₅₀ > 20000 L a Sha ER ₅₀ > 200.00 D a.s./ha	ESCORT &	2010b •
			NOBC repro200.00L		
predatory bug, Orius laevigatus	Acute contact, 24hr	@RD 460	$CLR_{50} > 200.0CL a.s. fa $	ESCORT &	, 2010c
			NOEO repro-200200 L a.s.ha		
plant dwelling insect,	Açute Contact, 24hr		$LR_{50} = 200.002$ a.s./hg	ESCORT	, 2010d
<i>Coccinella</i> Septempunctata L.			NOEC repro 200.00L		
Earthworms (IIA 8.9)					
Eisenia fetida	Acuto 4	QRDC452	LGS > 1000 mg test item/kg	OECD 207	2011
		Formutation	NQEC = 1000 mg test iten kg dry soil.		
- N					L]

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

QRD 452 volations 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.

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

unifier IIIA 10.11.3 Short and long term risks for non-target species, popplations, commu and processes

<text><text><text><text><text><text><text><text> In 10.11.5 Precartions necessary to avoid an injunize contamination of the environment.