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Risk assessment of Malakite with the active substances dithianon and pyrimethanil

Opinion of the Panel on Plant Protection Products of the Norwegian Scientific Committee for Food Safety

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Risk assessment of Malakite with the active substances dithianon and pyrimethanil

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Assessed and approved

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Competence of VKM experts

Persons working for VKM, either as appointed members of the Committee or as external experts, do this by virtue of their scientific expertise, not as representatives for their employers or third party interests. The Civil Services Act instructions on legal competence apply for all work prepared by VKM

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Summary

The plant protection product Malakite (BAS 669 01 F), containing the active substances dithianon and pyrimethanil, is a fungicide against scab in pome fruits. Products containing these active plant protection substances are approved in Norway, but not with both substances in the same product. The Swedish Chemicals Agency (KemI) has as zonal Rapporteur Member State (zRMS) of the Northern Zone evaluated the product Malakite and decided on non-approval due to the observation of unacceptable effects in exposed birds, aquatic organisms, non-target arthropods and earthworms.

On request from The Norwegian Food Safety Authority, the VKM Panel on Plant Protection Products has discussed the available data and the report prepared by KemI, and has concluded as follows on the questions raised:

On the refinement of DT50 in long term risk assessment for birds

It is the view of the VKM panel that the refinement is not acceptable because the analysis using first order kinetics seems not in line with a realistic and sufficiently conservative approach for the data provided. Furthermore, field studies from more sites are required.

On the long term cumulative effects of the active substances on birds

VKM shares the view of KemI, that the combined sub-lethal and reproduction effects should be assessed because the mode of action of the two ingredients has only been shown in fungi, and since the mechanisms in birds could be different.

On the reduction of assessment factor for fish

VKM opposes to the reduction of assessment factor for dithianon in fish because the data from acute toxicity tests cannot be extrapolated to chronic toxicity, and because the factor should reflect not only the variation in interspecies sensitivity, but also the uncertainty involved in extrapolation from laboratory tests to the field situation.

On the choice of end point in risk assessment for fish

The VKM panel considers the NOEC of dithianon for fish determined from the study at pH 7.9 not to be adequate for the more acidic Norwegian surface waters, and recommends using the data from the test performed at pH 6.5.

On the formulation studies for aquatic organisms

It is the opinion of the VKM panel that the formulation studies may be used together with corresponding studies with the active ingredients as long as the studies compared are performed and evaluated according to the same principles. However, VKM notes that the formulation tests as well as the tests of the active ingredients have been performed at high

pH values, which are not representative to most Norwegian surface waters. Thus, the toxic effect of dithianon shown in these tests are likely to be lower than expected under typical conditions in Norway.

On the assessment factors for concentration addition in fish

It is the opinion of the VKM panel that a reduction in assessment factor for one component in a mixture cannot be used for a formulation containing components for which a similar reduction has not been accepted.

On effect studies of active substances and formulations on non-target arthropods

The VKM panel shares the view of KemI that the risk assessment should be based on all available information, including the studies presented for the active substances.

On the endpoint in earthworm risk assessment

VKM supports the view of KemI that the observed effects of pyrimethanil on reproduction of earthworms should be considered in the risk assessment of Malakite.

Key words: VKM, risk assessment, Norwegian Scientific Committee for Food Safety, Malakite, pesticide, dithianon, pyrimethanil

Sammendrag på norsk

Malakite, som inneholder virkestoffene dithianon og pyrimetanil, er et nytt soppmiddel til bruk i steinfrukt. Andre plantevernmidler med disse aktive stoffene er godkjent i Norge, men ikke med begge stoffer i samme produkt. Den svenske Kjemikalieinspeksjonen (KemI) har evaluert produktet Malakite for EUs nordlige sone og besluttet å ikke godkjenne preparatet på grunn av uakseptable effekter for fugl, vannlevende organismer, leddyr og meitemark. På forespørsel fra Mattilsynet har VKMs Faggruppe for plantevernmidler vurdert tilgjengelige data og rapport utarbeidet av KemI, og har konkludert slik på de spørsmål som stilles:

Når det gjelder risikovurdering for fugl er det faggruppens oppfatning at den utførte analyse av nedbrytningshastigheten av dithianon i insekter som fuglene spiser ikke i tilstrekkelig grad er tilpasset dataene fra de eksperimentelle forsøkene, samt at flere feltstudier er nødvendig. VKM deler synet til KemI om at kombinerte effekter på fugl av de to virkestoffene bør vurderes siden mekanismene som stoffene virker ved kan være andre enn det som er vist i sopp.

VKM mener at det ikke er grunnlag for å redusere usikkerhetsfaktoren (Assessment factor AF) i risikovurderingen av langtidseffekter på fisk av dithianon slik som foreslått av tilvirker.

Ved valg av endepunkt for langtidseffekter av dithianon på fisk anser VKM at en studie utført med regnbueørret ved pH 7.9 er lite representativ for Norske forhold siden pH-verdien i overflatevann i Norge vanligvis er betydelig lavere. Dette er vesentlig fordi nedbrytningen av dithianon ved hydrolyse er mye langsommere ved lave pH-verdier enn ved pH 7.9. I stedet anbefaler VKM at en annen studie med regnbueørret ved pH 6.5 legges til grunn for risikovurderingen i Norge.

VKM mener at studiene av effekter på vannlevende organismer av formuleringen (Malakite) kan benyttes i sammeligning av effekter av de enkelte virkestoffene så lenge studiene er utført under like betingelser. VKM peker imidlertid på at de fleste studiene er utført ved høye pH-verdier, og at toksiske effekter av dithianon som er vist i disse studiene trolig er lavere enn man kan vente i de fleste Norske vannforekomster, hvor pH-verdien er lavere og dithianon mer stabil.

Ved beregning av samlet risiko for effekter på fisk ved summering av risikoen som de enkelte ingrediensene representerer må eventuelle forskjeller i usikkerhetsfaktorene for de ulike ingrediensene beaktes. VKM støtter ikke tilvirkers forslag å benytte den lavere usikkerhetsfaktoren for dithianon også for pyrimethanil.

VKM støtter KemIs holdning at all tilgjengelig, relevant informasjon om effekter av aktive ingredienser skal benyttes som grunnlag for risikovurdering av produktet. Dette gjelder for insekter, hvor enkelte arter synes å være mer følsomme enn de som er benyttet i tester av produktet. Videre må observerte effekter av pyrimetanil på reproduksjonen av meitemark tas hensyn til ved risikovurderig av produktet Malakite.

Abbreviations

MoA	Mode of Action
NOEC	No Observed Effect Concentration
EC50	50% Effect Concentration
LC50	50% Lethality Concentration
LoEP	List of Endpoints
zRMS	zonal Rapporteur Member State
KemI	Swedish Chemicals Agency
EFSA	European Food Safety Authority
DT50	Half-life time
HQ	Hazard Quotient
TWA	Time Weighted Average

Background as provided by the Norwegian Food Safety Authority

The plant protection product Malakite (BAS 669 01 F), is a fungicide (against scab in pome fruits) containing the active substances dithianon and pyrimethanil. Plant protection products containing these active substances are currently approved in Norway. The Swedish Chemicals Agency (KemI) has as zonal Rapporteur Member State (zRMS) of the Northern Zone evaluated the product Malakite and decided on non-approval due to unacceptable effects demonstrated in birds, aquatic organisms, non-target arthropods and earthworms.

Terms of reference as provided by the Norwegian Food Safety Authority

With regards to the comments presented by Sweden for the product Malakite, regarding the risk to birds, fish, non-target organisms and earthworms, Norwegian Food Safety Authority would like the VKM's scientific opinion on:

- The refinement of DT50 considering long term risk assessment for birds
- The (long term) cumulative effects of the active substances to birds
- The reduction of the assessment factor (long term risk assessment) for fish
- The choice of end point for the long-term risk assessment for fish
- Acceptability of the formulation studies for aquatic organisms
- The use of different assessment factors for calculation of concentration addition (According to the guidance document on work sharing in northern zone)
- The use of studies on active substances on non-target arthropods even if formulation studies have been submitted
- The use of endpoint for the active substance pyrimethanil in earthworm risk assessment

Assessment

1 Introduction

VKM has reviewed the Registration report on Malakite (BAS 669 01 F) for the Northern Zone prepared by BASF (2014) with review comments from KemI (Sweden), as well as the EFSA conclusion reports on the two active ingredients; pyrimethanil (EFSA 2006) and dithianon (EFSA 2010) as background for this opinion on the issues specified in the Terms of Reference.

2 Hazard identification and characterisation

VKM's assessment and conclusions on the issues raised by The Norwegian Food Safety Authority in relation to the Registration Report on Malakite for the Northern Zone are presented below.

2.1 The refinement of DT50 considering long term risk assessment for birds

The risk assessment indicated unacceptable long-term effects for small insectivorous bird at tier 1. At this tier, a default half-life (DT50) of 10 days was used for calculation of the concentration of dithianon in arthropodes on which the birds feed. In a higher tier reproductive risk assessment for blue tit, (*Parus caeruleus*), the applicant used a refined DT50 of 3.57 derived from a field experiment. With this refined DT50-value, the calculations indicated an acceptable risk.

The zRMS for the Northern Zone (KemI) did not accept the basis for refining of the DT50 due to the great variation in both maximum residues and the shapes of the dissipation curves between replicates. Furthermore, KemI is of the opinion that the applicant has not provided adequate information to support that the results from the field study, which was performed with a different formulation, could be applied to dithianon in Malakite.

VKM has reviewed the field study which provided the data for calculation of DT50 (BASF DocID. 2012/1017192), and the document which describes how the DT50 was derived from the field study data (BASF DocID. 2013/1068015).

VKM notes that the interpretation of the data from the field study is complicated by large variation in maximum residue levels in arthropods in different plots (replicates) and between repeated applications.

It is stated in the guidance document for risk assessment of birds and mammals (EFSA 2009), (Chapter 6.1.4.2 and Appendix N) that "…regarding initial (maximum) residue values, the maximum is often found some time later - not immediately after application of the test substance (especially substances non-toxic to arthropods may accumulate within the first few days after application). For a proper elucidation of the time courses of residues it is important to use an appropriate model to describe the residue decline. Normally it is not a first order kinetic, because several processes are interfering…". Further on, the guidance states that «summarising the area under the curve is the most suitable method to describe longer-term residue patterns for arthropods». The recommendation is that the particular way of providing data for refined exposure should represent a realistic, but sufficiently conservative approach. Furthermore, EFSA emphasizes that field studies are subject to much more natural variation than laboratory studies, so it is essential to conduct sufficient studies (at different sites and under varying conditions) to demonstrate that differences from the default values are statistically significant.

The field study clearly demonstrates the fact mentioned in the guideline that uptake of residues by arthropod populations occur over the first days after application takes place. The applicants' use of first order kinetics, and disregarding the absorption/distribution phase of uptake in arthropods is therefore not in line with a realistic and sufficiently conservative approach for providing the data, and should therefore be disregarded.

2.2 The long-term cumulative effect of the active substances for birds

VKM supports the view of KemI, that the sub-lethal effects and effects on reproduction of the active ingredients in birds should be assessed for the two active substances in combination, since the mode of action (MoA) of the two ingredients has only been demonstrated for fungi as target organism, and since the MoA for sub-lethal and reproductive effects in birds could be assumed to be different unless proven otherwise.

2.3 Assessment factors long term toxicity to fish (dithianon)

For the long-term risk assessment, the applicant has used the endpoint 3.9 µg/L (*Oncorhynchus. mykiss*) with a reduced assessment factor (AF) from 10 to 3, referring to the EFSA conclusion on dithianon (EFSA 2010). The arguments for reducing the AF were that the most sensitive species of 10 tested fish species in acute toxicity tests (*Ictalurus punctatus*, LC50 14.3) is a factor 3 more sensitive than *O. mykiss* (LC50 44 µg/L). Since chronic toxicity to fish has been tested only with two species, not including *I. punctatus*, the same factor 3

applied on the NOEC for *O. mykiss* was supposed to account for the difference in sensitivity between the tested species and the most sensitive species in chronic toxicity tests.

VKM opposes to the reduction of the AF for two reasons: 1) The difference in sensitivity between species found in acute toxicity tests cannot be extrapolated to chronic toxicity. 2) The AF is applied to account for the degree of uncertainty in extrapolation from laboratory toxicity tests data from a limited number of species to the 'real' environment. Thus, not only the interspecies sensitivity variation should be reflected by the AF.

2.4 Choice of endpoint for the long-term risk assessment for fish (dithianon)

The database of chronic effects of dithianon on fish contains NOECs from three tests with *O. mykiss* and one with *Gasterosteus aculeatus*. The lowest NOEC is 0.625 µg/L (nominal concentration) or 0.46 µg/L (measured initial concentration) from a 21 day flow-through test with *O. mykiss*, carried out at pH 6.5. In the EFSA conclusion on dithianon (EFSA 2010), a NOEC of 3.9 µg/L (measured initial concentration), obtained from a 79 day study applying pulsed exposure with *O. mykiss* was considered more relevant since this exposure pattern is more representative for the predicted environmental exposure of dithianon as a result of repeated applications. Also in the registration report for Malakite for the southern zone, the lower NOEC from the flow-through test was disregarded because the acidic conditions, which was claimed to cause unrealistic exposure and toxicity due to longer availability of dithianon. KemI, argues that for Sweden a pH of 6.5 is not uncommon and therefore this study should not be disregarded in the registration in Sweden.

VKM has reviewed the two chronic tests of dithianon on *O. mykiss* based on the test summaries included in the Draft Assessment Report prepared by Greece (2006). An overview of test design and results is shown in Table 2.4-1.

The effect concentrations in the flow-through test were reported as nominal concentrations, but in the LoEP these have been recalculated as measured, initial concentrations based on the average recovery (74%) in analysis of stock solutions and higher test concentrations. Thus the lowest NOEC (behaviour) is 0.46 µg/L expressed as measured, initial concentration.

The hydrolytic degradation of dithianon is strongly pH dependent and the available studies of hydrolysis at pH 5, 7 and 9 indicate an exponential decrease of DT50 from 12 days at pH 5 to 9.8 minutes at pH 9. Based on an exponential regression analysis of the data, the DT50 at the pH-values of the two long-term fish tests can be estimated at 0.93 days at pH 6.5 (the pH in the flow through test) and 0.068 days (100 minutes) at pH 7.9 (pulsed dosage test). Due to the difference in degradation rates as well as dosing procedure, the exposure pattern of the fish in the two tests is very different. In the flow-through test, the water exchange rate (approximately four times per day) was significantly higher than the estimated hydrolytic degradation rate at pH 6.5 and therefore maintenance of exposure concentrations close to the nominal concentrations would be expected throughout the test.

Table 2.4-1. Results and test design for two chronic tests of dithianon on *O. mykiss* .

Study id. (BASF DocID)	DT 512-002	DT 511-015
Test protocol	OECD 204	EEC 91/414
Design	Flow-through (retention 5.7 hours)	Pulsed dosage (each 7th day)
Duration	21 d	79 d
Fish length (start)	4.8 (4.2 - 5.4) cm	length 2.5 (2.4 - 2.6) cm
Fish weight (start)	1.2 (0.8 - 1.7) g	0.14 (0.12 - 0.16) g
No. of fish per treatment	10	20 (4x5)
pH	6.5 (6.3 – 6.8)	7.9 (7.6 – 8.2)
Exposure conc. (nominal)	0.156, 0.625, 2.5, 10, 40 µg/L	2, 4, 6, 12 µg/L
NOEC	0.625 µg/L (behaviour)	3.9 µg/L (mortality)*
NOEC mortality	2.5 µg/L	3.9 µg/L*
NOEC growth /length, weight	≥2.5µg/L	6.1 µg/L*

*measured, initial concentration

However, analytic measurements of dithianon at the nominal concentration 2.5 µg/l on day 1, 12 and 21 showed 61, 23.5 and 19.4% of the nominal concentration respectively. There may be several reasons for this deviation from the expected pattern, but the summary provides no explanation.

In the pulsed dosage test, the test solutions were replaced once a week. The initial measured concentrations were close to the nominal concentrations, but after seven days (before replacement of the solutions) the concentration of dithianon was below the detection level (0.2 µg/L) in all treatments. This is in agreement with the expected hydrolytic degradation of dithianon at pH 7.9. Under the conditions of this test, the concentration is expected to be less than 1% of the initial concentration after 12 hours. Since the pulsed dosage test was performed with sediment in the test containers, the concentration in the water phase may have been even lower due to adsorption of dithianon to the sediment.

As pointed out by the applicant, mortality was the most sensitive endpoint in the pulsed dosage studies performed with rainbow trout and stickleback, and sub-lethal effects, if any, were observed, within the next, higher test concentration without significant mortality. Furthermore, most of the mortality occurred within the first few days of the test in all these studies and the applicant concluded that repeated application of dithianon does not constitute a significantly higher risk to fish than a single application.

In the flow-through study at pH 6.5, sub-lethal effects (hypo-activity) were observed at a concentration that caused no mortality. This can probably be explained by the more prolonged exposure to dithianon as compared to the pulsed dosage studies. However, the

applicant has adopted the view expressed by EFSA in the conclusion report on dithianon (EFSA 2010), and considers the exposure situation in the flow-through study as unrealistic. Consequently the risk assessment has been based on the NOEC from the pulsed dosage study.

The reason that chronic toxicity was observed at sub-lethal concentrations in the flow-through test, but not in the pulsed dosage tests is, most likely, that sub-lethal, chronic effects require longer exposure duration than acute lethality. Thus, sub-lethal effects are often more related to the geometric mean or time weighted average concentration (TWA) than the peak concentration in fluctuating exposure situations. The rapid hydrolysis of dithianon that occurred in the pulsed dosage study at pH 7.9 caused peaks of very short duration and TWA has been estimated at only 1.6 % of the peak concentrations, which most likely is too low to cause sub-lethal chronic toxicity. A similar exposure pattern can be expected to occur in a water body with pH 7.9 receiving dithianon from multiple applications of Malakite at 8 days intervals. In this case the TWA can be estimated at 1% of the initial (peak) concentration. However, due to the strong influence of pH on the degradation rate, the estimated TWA increases to 3% of the peak concentration at pH 7.5, 6.6% at pH 7, 17% at pH 6.5 and 46% at pH6. Thus, the probability that chronic, sub-lethal toxic effects occur increases with decreasing pH-value of the receiving water. (In the flow-through test, where such effects were observed, the TWA was estimated at approximately 40% of the initial, peak concentration).

Analysis of all data on pH in Norwegian surface waters between 2010 and 2014 in the database of the Norwegian Environmental Agency shows that the median pH is 6.4, and 27% of the data points are below pH6. pH values ≥ 7.9, as in the pulsed dosage study, were found in less than 8% of the analysed samples (n=35501). The opinion of VKM is therefore that the NOEC from the pulsed dosage study (3.9 µg/L) does not sufficiently account for possible sub-lethal chronic effects on fish in water bodies with low pH, which receive dithianon from repeated applications of Malakite.

In conclusion, due to the high pH in the pulsed dosage study (DT 511-015) as compared to most Norwegian water bodies, the NOEC obtained from this study (3.9 µg/L) is not considered sufficiently conservative to protect against sub-lethal, chronic toxic effects on fish.

The pH-value in the flow-through study (DT 512-002) is relevant for Norwegian conditions, but the flow-through design creates an exposure pattern which is different from the predicted exposure that will occur in waterbodies influenced by repeated applications of dithianon. However, the average exposure concentration in the study were in the same range as the predicted average concentration in a water body at pH-values between 6.0 and 6.5, influenced by repeated applications of dithianon. VKM therefore recommends the use of the NOEC from the flow-through study (0.46 µg/L) as a basis for risk assessment in Norway.

2.5 Acceptability of formulation studies for aquatic organisms

The applicant has provided short term toxicity tests of the formulation Malakite on algae, Daphnia and fish. KemI has not accepted these formulation tests because the test endpoints (LC50, EC50) are based on nominal values even though the measured concentration of dithianon did not remain within 80-120 % of nominal concentrations during the exposure period.

The acute toxicity tests on algae, Daphnia and fish were all performed at a pH 8, i.e. under conditions where the half-life (DT50) of dithianon is expected to be less than 2 hours. This means that the exposure concentration in a static test will fall to less than 1% of the initial concentration already after 10 hours. Calculation of mean measured concentrations for exposure periods of 48h (Daphnia), 72h (algae) or 96 hours (fish) would yield extremely low effect concentrations of limited relevance for risk assessment.

The main purpose of the formulation tests is to identify any cumulative toxic effects of all ingredients in combinations, i.e. effects that are not covered by tests of the single components. Indications of cumulative effects (e.g. additive or synergistic), can be found by comparing results of the tests of the formulation with those of the individual components. Such comparison requires that the tests are performed and evaluated according to the same principles. In the case of dithianon, several data on acute toxicity to algae, Daphnia and fish are available. The toxicity data listed in the EFSA conclusion report are all referring to measured initial concentrations or (in some cases) nominal concentrations. In all these tests, it can be assumed that the exposure concentrations have declined to undetectable levels during the exposure period as they did in the formulation studies. Still, the toxicity data, expressed as measured initial concentrations have been accepted for risk assessment of the active ingredient.

The opinion of VKM is that the results from the formulation tests of Malakite are relevant for the assessment of cumulative toxicity of the formulation ingredients in the aquatic environment. However, VKM notes that the formulation tests as well as the tests of the active ingredients have been performed at high pH values, which are not representative to most Norwegian surface waters. Thus, the toxic effect of dithianon shown these tests are likely to be lower than expected under typical conditions in Norway.

2.6 Use of different assessment factors for calculation of concentration addition

In the acute formulation risk assessment for aquatic organisms, the applicant has used a reduced assessment factor (AF=10) for fish. This was based on the proposed reduction of AF for dithianon from 100 to 10 due to the fact that several species of fish have been tested, which implies reduced uncertainty with regard to interspecies sensitivity variation.

The opinion of VKM is that if a reduction of AF can be accepted for one component of a mixture, this cannot be carried over to a formulation also containing components for which a similar reduction of AF has not been accepted.

2.7 The use of studies on active substances on non-target arthropods even if formulation studies have been submitted

Only toxicity data derived from studies with the formulated product Malakite was used as basis for the risk assessment by the applicant. KemI has noted that toxicity data of the active substances listed in List of endpoints (LoEP) have not been taken into consideration. The risk assessment demonstrates acceptable risk at tier 1, in-field and off-field for non-target arthropods *Aphidius rhopalosiphi* and *Typhlodromus pyri* (HQ < 2). However, tests performed on the active ingredients indicate that some species are more sensitive than those used in tests of the formulation.

VKM supports the view of KemI that the risk assessment should be based on all available information, including the studies presented in the LoEP for the active substances, and product studies are not automatically given higher tier option compared to studies presented in LoEP.

2.8 The use of endpoint for the active ingredient pyrimethanil in earthworm risk assessment

The applicant has only referred to studies with the formulated product as basis for risk assessment. KemI has noted that the LoEP contains a NOEC= 4.12 mg/kg for effect of pyrimethanil on reproduction of earthworms. This is lower than the NOEC=32 mg/kg calculated from the formulated product BAS 605 04 F, and which is used by the applicant. KemI is of the opinion that formulation studies are not automatically a higher tier option compared to LoEP-data.

VKM supports the view of KemI that the available data on effects of pyrimethanil on reproduction of earthworms should be regarded in the risk assessment of the formulated product Malakite.

3 Conclusions with answers to the terms of reference

1. The field study clearly demonstrates the fact mentioned in the EFSA Guideline Document that uptake of residues by arthropod populations occur over the first days after application takes place. The applicants' use of first order kinetics, and disregarding the absorption/distribution phase of uptake in arthropods is therefore not in line with a realistic and sufficiently conservative approach for providing the data, and should therefore be disregarded. Furthermore, field studies at several sites are required to show that differences from the default values are statistically significant.

2. VKM supports the view of KemI, that the combined sub-lethal effects and effects on reproduction of the active ingredients in birds should be assessed as long as the mode of action (MoA) of the two active ingredients has only been demonstrated for the target organisms fungi, and the MoA for sub-lethal and reproductive effects in birds is assumed to be different unless proved otherwise.

3. VKM does not consider the NOEC for long term toxicity of dithianon to fish from the pulsed dosage study performed at pH 7.9 to be sufficiently conservative to protect from sub-lethal toxic effects on fish in the more acidic Norwegian surface waters. VKM recommends to base the risk assessment for Norway on the NOEC from the flow-through test performed at pH 6.5 (0.46 µg/L).

4. VKM opposes to the reduction of the assessment factor (AF) for long-term effects of dithianon in fish for two reasons: 1) The difference in sensitivity between species found in acute toxicity tests cannot be extrapolated to chronic toxicity. 2) The AF is applied to account for the degree of uncertainty in extrapolation from laboratory toxicity tests data from a limited number of species to the 'real' environment. Thus, not only the interspecies sensitivity variation should be reflected by the AF.

5. The opinion of VKM is that the results from the formulation tests of Malakite are relevant for the assessment of cumulative toxicity of the formulation ingredients in the aquatic environment, as long as the formulation tests and the tests of the

single active ingredients have been performed and evaluated according to the same principles. However, VKM notes that the formulation tests as well as the tests of the active ingredients have been performed at high pH values, which are not representative to most Norwegian surface waters. Thus, the toxic effect of dithianon shown in these tests is likely to be lower than expected under typical conditions in Norway.

6. The opinion of VKM is that if a reduction of AF can be accepted for one component of a mixture, this cannot be carried over to a formulation also containing components for which a similar reduction of AF has not been accepted.

7. VKM supports the view of KemI that the risk assessment for non-target arthropods should be based on all available information, including the studies presented in the LoEP for the active substances, and product studies are not automatically given higher tier option compared to studies presented in LoEP.

8. VKM supports the view of KemI that the available data on effects of pyrimethanil on reproduction of earthworms should be regarded in the risk assessment of the formulated product Malakite.

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Appendix

OECD REVISED DRAFT FISH TOXICITY TESTING FRAMEWORK (2011)

The main difference of EU pesticides requirements (EU 2002) from the US pesticide legislation (USEPA 1972) and other jurisdictions is that short-term toxicity data from a 14 day prolonged study (OECD TG 204) may occasionally be requested as a supplement to (or in place of) OECD TG 203, but this is quite rare (and TG 204 will not be requested according to the upcoming guidance document (EU 2010)). More often, the EU accepts chronic data on juvenile fish growth (OECD TG 215), or even data from the embryo and sac fry test (OECD TG 212) under the Biocidal Products Directive (EU 1998), although the ELS (OECD TG 210) is still the preferred method of predicting true chronic toxicity, and is generally considered more sensitive than both OECD TG 212 and TG 215.

(OECD TG 204 was excluded from the Guidelines in 2014)