Conclusion regarding the peer review of the pesticide risk assessment of the active substance

acequinocyl

finalised: 17 December 2007

(revision of 10 January 2008 with minor editorial changes)

SUMMARY

Acequinocyl is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[1] the Netherlands received an application from Agro-Kanesho for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2003/636/EC[2].

Following the agreement between the EU-Commission and the EFSA for the EFSA to organise a peer review of those new active substances for which the decision on the completeness of the dossier had been published after June 2002, the designated rapporteur Member State the Netherlands made the report of its initial evaluation of the dossier on acequinocyl, hereafter referred to as the draft assessment report (DAR), available on 8 March 2005. This draft assessment report was distributed for consultation to the Member States and the notifier on 15 March 2005.

The peer review was initiated on 15 March 2005 by dispatching the draft assessment report for consultation of the Member States and the notifier. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting in November 2005. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in November 2006.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 15 November 2007 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as acaricide as proposed by the notifier which comprise foliar spraying to control spider mite in ornamentals, apples and pears. Full details of the GAP can be found in the attached end points.

[1] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by Commission Directive 2007/52/EC (OJ L 214, 17.8.2007, p.3)
[2] OJ No L 221, 4.9.2003, p.42

The representative formulated product for the evaluation was “Kanemite”, a suspension concentrate (SC) containing 164 g/L acequinocyl, provisionally registered in Austria and Germany as Kanemite and in the Netherlands as Cantack.

The technical specification is still open for formal reasons. A new specification was submitted and presented in an addendum to vol.4 according to the requirements of the expert meeting PRAPeR6, however, this final specification was not peer reviewed.

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

Regarding the mammalian metabolism, there are distinct indications for sizeable biliary first pass elimination. However, based on the critical effect of acequinocyl, the extent of oral absorption was considered to represent 28% of the administered dose. Twenty-four hours after dosing, the highest concentrations of radioactivity were found in the gastro-intestinal tract and its contents; excretion occurs predominantly via faeces and no potential for accumulation was seen. Acequinocyl is extensively metabolized with 0-2.5% parent compound found in urine, bile or faeces.
Acequinocyl has low acute toxicity and is not a skin or eye irritant; however classification is required for skin sensitization based on a Maximisation test. In repeated dose studies, acequinocyl caused haematological effects (increased platelet levels and blood clotting time) in rats, mice and dogs; in addition, ocular effects were observed in the rats and hepatotoxicity in mice. The relevant short term NOAEL was the dose level of 5 mg/kg bw/day derived from the 52-week dog study, and the long term relevant NOAEL was the dose level of 2.3 mg/kg bw/day derived from the 2-year rat study. No genotoxic or carcinogenic potential was observed. Acequinocyl showed no effect on fertility parameters and produced effects on the reproductive or developmental parameters in rats or rabbits only at parental toxic doses. No potential for neurotoxicity was evidenced. Four acute studies in rats and monkey were submitted to investigate the effects of acequinocyl on the blood clotting system resulting in an overall NOAEL of 8 mg/kg bw for prolongation of blood clotting time in rats.
The acceptable daily intake (ADI) is set at 0.023 mg/kg bw/day and the acute reference dose (ARfD) at 0.08 mg/kg bw considering an assessment factor of 100; the acceptable operator exposure level (AOEL) is set at 0.014 mg/kg bw/day considering an assessment factor of 357 (correction of 28% for oral absorption). Dermal absorption is 3.6% when handling the concentrate formulation and 16.7% when handling the spray dilution. Considering the representative uses of Kanemite SC outdoor (apple/pear and ornamentals), the estimated operator exposure exceeds the AOEL according to the UK POEM model; according to the German model calculations, exposure is below the AOEL when the use of PPE as protective gloves during mixing/loading and gloves, protective garment and sturdy footwear during application is considered. According to the Dutch model for greenhouse applications (ornamentals), the exposure of operators was calculated to represent twice the AOEL when using a reduction factor of 10% for the use of PPE. Worker exposure after outdoor applications on apple and

pear (mechanical upward spraying) is estimated to be below the AOEL even without the use of PPE, but for downward application on ornamentals, outdoor and in greenhouses, the use of gloves is required to obtain a level of exposure lower than the AOEL. Exposure of bystanders is estimated to be below the AOEL.

The metabolism of acequinocyl in fruit crops is clearly elucidated. For PHIs up to 30 days, the parent compound is the major constituent of the residue and no metabolite was found in amounts suggesting a significant contribution to the toxicological burden. The residue definition for monitoring and risk assessment can therefore be restricted to acequinocyl. Supervised residue trials were performed in Northern and Southern Europe and form a sufficient basis for proposing an MRL to be set at 0.05 mg/kg in apples and pears.
Considering this low residue level, no study on the effect of processing was estimated necessary.
No information has been provided on the potential transfer of soil residues to rotational or succeeding crops considering that cultivation of edible agricultural or horticultural crops in rotation with the representative uses does not normally occurs in practice. In case this should be possible practice at national level, Member States should consider the opportunity of label restriction.
A metabolism study in lactating goat was submitted although not required given that livestock exposure through consumption of apple pomace is extremely low. This study was considered but not used for proposing a residue definition.
Consumer chronic and acute exposures are well below the toxicological reference values and no dietary risk is expected resulting from the use of acequinocyl following the supported representative uses.

In soil under aerobic conditions acequinocyl exhibits very low to low persistence. The major metabolite was R1[3] (max 33.8% AR after 2 days) which exhibits low to moderate persistence. A second major metabolite was identified as AKM-18[4] (max 21.9% AR after 2 days), which showed low persistence in soil. Mineralisation to carbon dioxide accounted for 15.0-57.7 % AR after 120/180 days. The formation of unextractable residues was also a significant sink accounting for 46.3% AR after 120 days. Under anaerobic soil conditions no novel breakdown products were identified.
Acequinocyl and its major metabolites can be classified as immobile in soil and have a very low potential for leaching in soil. There was no indication that adsorption of either acequinocyl or metabolites R1 and AKM-18 was pH dependant.
Hydrolysis is pH dependant with more rapid hydrolysis under alkaline conditions. The water/sediment test showed that acequinocyl dissipated rapidly from the water phase by partitioning to sediment (max 26.4% AR after 1d). Unextracted sediment residues were a significant sink for radioactivity, representing 59.7-62.0% R after 30-60 days. Metabolites R1 and CBAA[5] were detected as major metabolites in the water phase, metabolite AKM-18 is a major metabolite in the sediment

[3] R1: 2-dodecyl-3-hydroxynaphthalene-1,4-dione; also referenced in the DAR as AKD-2023-OH, AKM-05, HDNQ
[4] AKM-18: 2-(2-oxotetradecanoyl)benzoic acid; also referenced in the DAR as F1
[5] CBAA: 2-(carboxycarbonyl)benzoic acid

phase. Predicted environmental concentrations in surface water to be used in the risk assessment for the representative uses form the spray drift route of exposure have been calculated for acequinocyl (actual and TWA PECsw) and metabolites R1 and CBAA (maximum PECsw). The runoff and drainage routes of exposure to surface water bodies should be taken into account by MS when these routes of exposure are relevant and the pertinent risk assessments to aquatic organisms should be completed by MS.
For the representative uses proposed by the applicant, the potential for contamination of vulnerable groundwater by acequinocyl and its soil breakdown products above the drinking water limit of 0.1 µg/L is considered minimal.

The acute and short-term risk to birds and the acute risk to mammals was assessed as low in the first-tier risk assessment. A refined long-term risk assessment for birds and mammals was required. The suggested refinement steps were rejected in the experts meeting. The long-term TER of 4.3 for insectivorous birds in orchards was below the trigger of 5 but considered as sufficient to conclude on a low risk since the available information on residue decline in insects suggest a rapid decline with a DT_{50} of <3 days. A data gap was identified to refine the long-term risk to herbivorous and insectivorous birds for the use in ornamentals. The PT values proposed to refine the long-term risk to mammals were rejected because no supporting data were made available.
Acequinocyl is very toxic to aquatic invertebrates. In the meeting of experts it was agreed that the aquatic risk assessment should be based on the NOEC (population effects) of 3 µg acequinocyl/L derived from a microcosm study together with an assessment factor of 3-5. No spray buffer zones of 30 m (orchards late application and ornamentals >50 cm high) and 10 m (ornamentals <50 cm high) are required to achieve TERs of >5. In order to reach a TER of >3 for the early use in orchards a no spray buffer zone of 30 m is required and the buffer zone needs to be extended to 50 m to achieve a TER of >5.
The risk to bees, other non-target arthropods, earthworms, other soil non-target macro- and micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.

Key words: acequinocyl, peer review, risk assessment, pesticide, acaricide, insecticide

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BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC the Netherlands received an application from Agro-Kanesho for inclusion of the active substance acequinocyl in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2003/636/EC.

Following the agreement between the EU-Commission and EFSA for EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the designated rapporteur Member State the Netherlands submitted the report of its initial evaluation of the dossier on acequinocyl, hereafter referred to as the draft assessment report (DAR), to the ECCO team at the Federal Biological Research Center for Agriculture and Forestry (BBA) in Braunschweig on 8 March 2005. This draft assessment report was distributed for consultation to the Member States and the notifier on 15 March 2005.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 29 November 2005 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier was attending this meeting.

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

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 15 November 2007 leading to the conclusions as laid down in this report.

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

Following the agreement between the EU Commission and EFSA regarding the peer review of new active substances, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

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

- the comments received,
- the resulting reporting table (rev. 1-1 of 20 December 2005)

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

- the reports of the scientific expert consultation,
- the evaluation table (rev. 2-1 of 15 November 2007).

Given the importance of the draft assessment report including its addendum (compiled version of September 2007 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

By the time of the presentation of this conclusion to the EU-Commission, the rapporteur Member State has made available amended parts of the draft assessment report (Vol. 3, B1-B9 and Vol. 4) which take into account mostly editorial changes. Since these revised documents still contain confidential information, the documents cannot be made publicly available. However, the information given can be found in the original draft assessment report together with the peer review report, both of which are publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Acequinocyl is the ISO common name for 3-dodecyl-1,4-dihydro-1,4-dioxo-2-naphthyl acetate (IUPAC).

Acequinocyl is an unclassified acaricide. Acequinocyl blocks the cellular respiration at membrane level by inhibiting the Qo centre of Complex III in the membranes of mitochondria of mites. It blocks the membrane electron transport. It is used as foliar application to control spider mites in ornamentals, apples and pears.

The representative formulated product for the evaluation was "Kanemite", a suspension concentrate (SC) containing 164 g/L acequinocyl, provisionally registered in Austria and Germany as Kanemite and in the Netherlands as Cantack.

The representative uses evaluated comprise field and greenhouse foliar spraying to control *Tetranychus urticae* in ornamentals, up to a maximum one treatment in outdoor use, and maximum 3 treatments in greenhouses, at a maximum application rate per spray of 150-600 g as/ha at a 7 day interval between applications in greenhouses and also foliar spraying to control *Panonychus ulmi* in

apples and pears up to a maximum one treatment, at a maximum application rate per spray of 150-280 g as/ha.
The outdoor uses in ornamentals, apples and pears require further considerations.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of acequinocyl as manufactured cannot be given at the moment, as the specification of the technical material requires clarifications. No FAO specification exists.
A new technical specification was presented in an addendum to Vol. 4, however, the experts of the PRAPeR 6 meeting required further explanation and set a data gap to provide a new technical specification. The proposed minimum a.s. content of 962 g/kg is the minimum value measured in the five batch, and clarification is also needed on the specification of the impurities, in particular the sum of volatiles and the explanation of specifying a non relevant impurity below 1 g/kg. However the open specification is not considered to be a critical area of concern. A new specification was submitted and presented in a revised addendum to volume 4 with a proposed minimum a.s. content of 960 g/kg, which fulfils the requirements from the PRAPeR 6 meeting. However, this final specification was not peer reviewed.
In a late stage of the evaluation of the acequinocyl dossier, it became clear that the concentration of the active substance in the formulation Kanemite is not 150 g/L but 164 g/L. A revised specification of the preparation was required and submitted in an addendum to vol. 4
RMS confirmed that the use (i.e. g/ha and g/hL) in the table of intended uses is correct and consequent with the change in formulation concentration. The change in the a.s. content of the formulation was not considered a critical area of concern as all risk assessments in the DAR are based on the maximum amounts of acequinocyl per hectare and these amounts have not changed.
The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of acequinocyl or the formulation.

The main data regarding the identity of acequinocyl and its physical and chemical properties are given in appendix 1.

Adequate methods of analysis are available for the determination of acequinocyl in technical material and in formulations. Validated methods are available for the determination of impurities in technical acequinocyl.

Sufficiently validated methods for acequinocyl and its metabolite R1[6] in apples, oranges, egg-plants and grapes with an LOQ of 0.01 mg/kg are available, as well as for animal matrices. Some methods are available also for the determination of acequinocyl and its metabolite R1 in milk and animal tissues (beef muscle, liver, kidney, fat), however an analytical method for food of animal origin is not required due to the fact that no residue definition is proposed.

The applicability of the multi-residue method DFG method S19 for the determination of acequinocyl and its metabolite was tested and it was concluded that no multi-residue method using GC(MS) is possible for the determination of acequinocyl and hydroxy-acequinocyl in the respective plant and animal matrices.

Validated analytical methods based on HPLC-MS/MS exist for the determination of acequinocyl, metabolites R1 and AKM-18[7] in soil with a LOQ of 0.01 mg/kg. For the determination of residues of acequinocyl and R1 in ground- and surface water an HPLC-MS/MS method exists with an LOQ of 0.1 µg/L.

Validated HPLC-MS/MS exists for the determination of acequinocyl and metabolite R1 in air with a LOQ of 0.075 mg/m^3.

Adequate methods are available to monitor acequinocyl given in the respective residue definitions in food of plant origin, in soil, water and in air.

2. Mammalian toxicology

Acequinocyl was discussed at the PRAPeR Expert's Meeting on mammalian toxicology (PRAPeR 9) in November - December 2006.

Specification of the active substance presented in an addendum do volume 4 in October 2006 was checked and agreed on from the toxicological point of view. New specification presented in an addendum to volume 4 in September 2007 was not peer reviewed, however does not change the conclusions of the experts.

Acequinocyl and most of its identified metabolites are structure analogues of vitamin K. Therefore, its mechanism of toxicity is probably competitive inhibition of the vitamin K dependent prothrombin synthesis.

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

Oral absorption is considered to represent 28% of the administered dose (10 mg/kg bw/day), based on urinary excretion, biliary excretion, cage wash and residual carcass after 48 hours. Saturation of absorption and retardation of faecal excretion were observed at the high dose level (500 mg/kg bw). Twenty-four hours after dosing, the highest concentrations of radioactivity were found in the gastro-intestinal tract and its contents, and intermediate concentrations were found in fat, kidneys, liver, lungs, lymph nodes and pancreas. There was no potential for accumulation. Excretion occurred predominantly via faeces (87% in faeces and 13% in urine after 120 hours); within the first twenty-

[6]R1: 2-dodecyl-3-hydroxynaphthalene-1,4-dione; also referenced in the DAR as AKD-2023-OH, AKM-05, HDNQ

[7] AKM-18: 2-(2-oxotetradecanoyl)benzoic acid; also referenced in the DAR as F1

four hours after low dose, approximately 75% of the administered dose had been excreted, while after high dose excretion had been around 40%.

Metabolism pattern was different in bile and in urine, giving indications for sizeable biliary first-pass effect. Parent compound and two of the five identified metabolites appeared in bile and faeces, but not in urine. AKM-14[8] and AKM-15[9] were identified as the main metabolites in urine, while no parent was detected. The main faecal metabolites were R1 and AKM-18, while the main metabolite in bile was identified as a glucuronide conjugate of R1. Two and 2.5% parent compound were found in faeces and bile, respectively.

2.2. ACUTE TOXICITY

The acute toxicity of acequinocyl is low. In the acute inhalation toxicity study, inflammatory reactions have been observed in the lung, which was considered to be caused by the physical-chemical properties of the soap-like compound. The experts concluded that the application of a safety phrase might be required based on this finding, however this decision has to be taken by the competent authority for classification and labelling. Acequinocyl is not a skin or eye irritant, but has to be proposed for classification as a **skin sensitizer** according to a Maximisation test.

2.3. SHORT TERM TOXICITY

The short term effects of acequinocyl were studied in three dietary range-finding 28-day studies (rat, mouse and dog), three 13-week studies (dietary in rat and mouse, and by gelatine capsule in dog) and one 52-week study in dog. A dermal 28-day study in rat was presented, but no study on repeated inhalation was available.

Repeated oral doses of acequinocyl produced haematological effects in the three species (increased blood clotting time and platelet count). Additionally, haemorrhage in the eyes was observed in rats and hepatotoxicity in mice (increased liver weights and hepatocytes vacuolation) that were noted from the lowest dose level of 16 mg/kg bw/day. A higher NOAEL for the 52-week dog study was proposed in the addendum than the one considered in the DAR. The NOAEL was discussed in the light of the increased platelet levels observed at 20 mg/kg bw/day and up. A decrease of coagulation was observed, that was proposed to be the critical effect. Taking into account the 13-week dog study, an increase of platelets has been observed, which was considered to be probably a secondary reaction to an unknown adverse effect. Therefore the experts considered the NOAEL to be the 5 mg/kg bw/day dose level, as was originally proposed in the DAR. This NOAEL was considered as the most relevant for oral short term toxicity.

In a 28-day dermal toxicity study in rat, the NOAEL was set at 200 mg/kg bw/day, based on increased partial thromboplastin time, prothrombin time and fibrinogen levels, and heart changes at 1000 mg/kg bw/day.

[8] AKM-14: 4-(3-hydroxy-1,4-dioxo-1,4-dihydronaphthalen-2-yl)butanoic acid
[9] AKM-15: 6-(3-hydroxy-1,4-dioxo-1,4-dihydronaphthalen-2-yl)hexanoic acid

2.4. GENOTOXICITY

Acequinocyl was tested *in vitro* for point mutations in an Ames test with *S. typhimurium* and *E. coli*, for chromosome aberrations in Chinese hamster lung cells and for gene mutations in mouse lymphoma cells L5178Y, and *in vivo*, in a mouse bone marrow micronucleus test. The mouse lymphoma assay was discussed in detail as presented in an addendum, and the meeting agreed that this test, as well as all the other genotoxicity tests presented show negative results.

2.5. LONG TERM TOXICITY

There was a distinct difference in the nature of chronic toxicity caused by acequinocyl in rats and mice.

In rats, chronic exposure caused increased number of platelets at 9 mg/kg bw/day onwards, and prolongation of clotting time and ocular effects from doses of 36 mg/kg bw/day onwards. As the target is blood and haemorrhagic effects were observed in the eye, these effects were concluded to be severe by the experts, however no classification was proposed as the benchmark for classification was exceeded. The NOAEL was the dose level of 2.3 mg/kg bw/day (50 ppm).

In mice acequinocyl caused liver and kidney toxicity. The experts agreed to set the NOAEL at the dose level of 2.7 mg/kg bw/day (20 ppm) based on relevant increase in the incidence of brown pigmented cells, inflammatory cells and generalised fat in the liver, as well as increased liver enzyme activity at the higher dose level of 7.0 mg/kg bw/day. No carcinogenic potential was observed from acequinocyl dosing neither in rats nor in mice.

2.6. REPRODUCTIVE TOXICITY

A rat multigeneration study and two developmental studies in rat and rabbit were presented in the DAR.

In the 2-generation reproduction study, the parental NOAEL was set at 6.9 mg/kg bw/day (100 ppm) based on treatment-related haemorrhages and protruding eyes at the higher dose level of 56 mg/kg bw/day onward. The developmental NOAEL was the same dose level of 6.9 mg/kg bw/day based on haemorrhagic effects and delayed physical and functional development before weaning. No fertility effects were observed and the NOAEL for fertility was therefore higher than 107 mg/kg bw/day (1500 ppm).

In a developmental study in rat, the maternal NOAEL was set at 150 mg/kg bw/day due to haemorrhagic effects and thin blood observed in the animals at 500 mg/kg bw/day and higher. The developmental NOAEL was set at 500 mg/kg bw/day based on the increased number of major abnormalities observed at the highest dose in presence of severe maternal toxicity.

The developmental study conducted in rabbits resulted in clinical signs and pathological findings including intra-uterine haemorrhage, pale liver and lungs, blood in the urine and resorption of foetuses at the top dose level of 120 mg/kg bw/day. A statistically significant increase in the number of 13th ribs was observed in offsprings of females in the highest dose group and was considered by the experts to be a transient effect of development that may be related to the observed maternal toxicity rather than a direct effect of the test substance. The meeting discussed the slight, not statistically

significant increase of extra 13th rib observed at the 60 mg/kg bw/day dose group and considered that it was not clearly treatment-related and not adverse. Therefore both the developmental and maternal NOAEL were set at 60 mg/kg bw/day based on the above mentioned effects.
Acequinocyl produced developmental effects only in the presence of maternal toxicity and does not require classification relating to reproduction or developmental toxicity.

2.7. NEUROTOXICITY

No study was conducted. Acequinocyl does not belong to chemical groups known to induce neurotoxicity; no concern was raised from the other general studies, and therefore no study is required.

2.8. FURTHER STUDIES

Four mechanistic studies were presented in the DAR (three were conducted in rat and 1 with rhesus monkey), as well as acute toxicity and genotoxicity studies with the metabolites AKM-18 and R1. These metabolites were produced from acequinocyl dosing in the rat (see point 2.1).

Mode of action: acute effects on blood clotting

Single administration of acequinocyl in doses ranging from 20 to 600 mg/kg bw to rats caused transient prolongation of blood clotting time as measured by the blood partial thromboplastin time (PTT) and prothrombin time (PT) tests. The effects appeared within 1 to 6 hours after administration, reached a peak at 24 hours and had ceased after 48 hours. Based on the three studies conducted in rat, an overall NOAEL of 8 mg/kg bw could be derived for this effect.
The study on monkeys produced minor increases in PT and PTT at a 1000 mg/kg bw dose level; however no well founded conclusion on the presence or absence of a toxicologically relevant effect could be drawn, as the uptake of the test substance was limited due to the reaction of the monkeys to dosing (vomiting, loose/liquid stool).

Metabolites

Metabolite AKM-18 presented an oral LD_{50} higher than 5000 mg/kg bw in mice; two in vitro genotoxicity studies (point mutation in *S. typhimurium* and *E. coli*, and chromosome aberrations in Chinese hamster lung cells) were negative.
In rat, **metabolite R1**[10] presented an oral LD_{50} higher than 5000 mg/kg bw and a dermal LD_{50} higher than 2000 mg/kg bw. No conclusion could be drawn from the genotoxicity studies in vitro (point mutation in *S. typhimurium* and E. coli, and chromosome aberrations in Chinese hamster lung cells) as the range of concentration used exceeded the precipitation level of the test substance; but an in vivo mouse bone marrow micronucleus assay gave negative results.

[10] Referenced in the DAR as AKM-05

2.9. MEDICAL DATA

Limited information is available as acequinocyl is a new active substance. No evidence of acute or chronic poisoning of employees involved in the manufacturing process of acequinocyl was shown over a period of three years.

2.10. ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) AND ACUTE REFERENCE DOSE (ARFD)

ADI

The **ADI for acequinocyl was established at 0.023 mg/kg bw/day** based on the NOAEL of 2.3 mg/kg bw/day from the combined chronic toxicity/carcinogenicity study in rats and an assessment factor of 100.

AOEL

Initially in the DAR, the Rapporteur Member State proposed the setting of exposure related specific AOELs (subacute, semi-chronic and chronic AOEL-systemic) considering the different types of application of acequinocyl. The experts discussed whether different values should be established for the assessment of re-entry workers exposure and whether different values should be developed for workers and operators. The meeting agreed that one AOEL would cover all representative uses reported in the DAR for operators and workers. The experts considered that the decrease of coagulation was a severe effect, being observed during acute and long term exposure.

The AOEL was set at 0.014 mg/kg bw/day, based on the NOAEL of 5 mg/kg bw/day from the 1-year dog study, which was supported by the two-generation study in rat, considering a safety factor of 100 and a correction factor for oral absorption of 28% (overall assessment factor of 357).

ARfD

The ARfD was set at 0.08 mg/kg bw, considering the overall NOAEL for blood clotting effects of 8 mg/kg bw from the mechanistic studies in rat upon single exposure, and an assessment factor of 100.

2.11. DERMAL ABSORPTION

An *in vitro* dermal absorption study with rat and human skin and an *in vivo* dermal penetration study in rat were presented in the DAR; both studies were conducted with the active substance diluted in a blank formulation.

Based on these studies, the experts agreed with the values for dermal absorption of 3.6% when handling the undiluted formulation Kanemite SC and of 16.7% for the spray dilution as proposed by RMS in the DAR.

Comparison of metabolite profiles resulting from the dermal and oral route of administration indicated that there were quantitative and qualitative metabolic differences between the two routes of exposure.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Kanemite SC is a suspension concentrate formulation (SC) containing 164 g acequinocyl/L for use in apple and pears (mechanical upward spraying) at a maximum application rate of 281 g acequinocyl/ha, and in ornamentals (manual downward spraying in glasshouse or outdoor applications) at a maximum application rate of 600 g acequinocyl/ha.

Operator exposure

According to the UK POEM model calculations, operators would be exposed to levels corresponding to about three times the AOEL, either in ornamentals (outdoor field application) or in apple/pear, when using the maximum protective equipment proposed in this model (protective gloves during mixing/loading and application).

According to the German model, exposure of operators was below the AOEL for both ornamentals (outdoor) and apple/pear, only if PPE (protective gloves during mixing/ loading, and gloves, protective garment and sturdy footwear during application) were used.

The Dutch model calculations for greenhouse application of acequinocyl in ornamentals (90th percentile) resulted in an estimated level of exposure of about twice the AOEL when using PPE (protective gloves and coverall during mixing/loading and application).

Estimated operator exposure presented as % of AOEL (0.014 mg/kg bw/day) after application of Kanemite SC, according to calculations with the UK POEM model, German model and Dutch model for greenhouse application. The default for body weight of operator is 60 kg for UK POEM and 70 kg for the German model.

Tractor-mounted, high crops (apple/pear)	No PPE	With PPE [(a)]
UK POEM (75th percentile)	645	343
German model (geometric mean)	465	69

Hand held knapsack sprayer (ornamentals)	No PPE	With PPE [(a)]
UK POEM (75th percentile)	786	317
German model (geometric mean) [(b)]	886	89

Hand held greenhouse (ornamentals) [(c)]	No PPE	With PPE [(d)]
Dutch model (90th percentile)	2102	210

[(a)] PPE for UK POEM: gloves during mixing/loading and application;
PPE for German model: gloves during mixing/loading, and gloves, protective garment and sturdy footwear during application;

[(b)] As the hand held German model is based on an upward spraying, the estimated exposure is a worst case scenario compared to the downward spraying intended for ornamentals.

[(c)] No suitable module available in the UK POEM or the German model

[(d)] PPE according to the Dutch model: protective gloves and coverall during mixing/loading and application (default reduction factor for PPE is 10%).

Worker exposure

Worker exposure was estimated using two exposure studies; additionally the draft values proposed for the EUROPOEM II model (2002) were used. Worker exposure was estimated to be below the AOEL after mechanical upward applications (apple/pear) even without the use of PPE. For downward applications (ornamentals, outdoor and in greenhouses), worker exposure was below the AOEL when the use of PPE (gloves) was considered.

Estimated worker exposure presented as % of AOEL (0.014 mg/kg bw/day)

Worker exposure	No PPE	With PPE [(a)]
After mechanical upward spraying (re-entry day 3) [(b)]	31	3
After mechanical upward spraying (re-entry day 0) [(b)]	39	4
After manual downward spraying (ornamentals)	500	50
After manual downward spraying (greenhouse)	500	50

[(a)] PPE: protective gloves
[(b)] As the pre-harvest interval is 30 days, re-entry exposure after 0-3 days concerns only inspections, which are considered to represent 1 hour exposure period (instead of the default 6 hours work rate).

Bystander exposure

As an estimate for bystander exposure, values proposed for the EUROPOEM II (2002) were used, representing the 90th percentile exposure. Outdoor applications of acequinocyl resulted in exposure of bystanders below the AOEL.

Estimated bystander exposure presented as % of AOEL (0.014 mg/kg bw/day)

	Tractor-mounted, high crops (apple/pear) applications	Hand held knapsack sprayer (ornamentals) applications
Bystander exposure	48	10

No estimate was performed on the exposure of bystanders for the greenhouse applications. The presence of bystanders should not be allowed in greenhouses during acequinocyl application.

3. Residues

Acequinocyl was discussed at the PRAPeR experts' meeting for residues in November 2006 (PRAPeR 10, Round 2).

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of acequinocyl has been investigated in apples, egg plants and oranges representing three fruit crops. These studies were performed after spray application and the metabolic pattern was

determined at a PHI of 30 days in apples and oranges, in accordance with the supported representative use in apples and pears.

The metabolic pathway of acequinocyl proceeds through hydrolysis of the acetic acid ester moeity, opening of the naphthalenedione ring and hydrolysis of the dodecyl aliphatic chain. These reactions result in the formation of phthalic acid. At the intended PHI of 30 days the parent compound represents about 50 % of the extractable radioactivity. Beside phthalic acid, 2 metabolites, present at levels one order of magnitude lower than the parent compound were identified: R1[11] and AKM-18[12]. Other metabolites, also present at low levels were only characterized.

The residue definition proposed for monitoring and risk assessment is acequinocyl. Metabolites R1 and AKM-18, although considered as structure analogues of vitamine K and therefore of a similar level of toxicity as the parent compound, do not need to be included in the residue definition. They are present in the rat metabolism, and due to their low relative amounts are not expected to increase significantly the toxicological burden of the parent compound. Phthalic acid was not considered appropriate for inclusion in the residue definition, due to its lack of specificity and its presence in the environment from other sources.

A sufficient number of supervised residue trials (8 trials in Northern region and 10 trials in Southern region) have been performed supporting the representative use in pome fruits. Residues were similar in both regions. In Southern region the highest residue (HR) found was 0.030 mg/kg and the supervised trial median residue (STMR) amounted to 0.014 mg/kg. In Northern region these values were 0.042 mg/kg and 0.011 mg/kg respectively. In addition metabolite R1 was also analysed in the trials and as expected from metabolism studies its levels were below that of parent.

These results can be considered as reliable as storage stability studies demonstrated that residues of acequinocyl and its metabolite R1 are stable in high water content matrices under deep freeze conditions for at least 18 months.

No studies were submitted by the applicant on the effect of processing on the nature and the level of residues. Considering the low residue levels in raw commodities as well as the fact that the consumer exposure is low in comparison to toxicological reference values, these studies are not required.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Studies on the potential for residues to be present in rotational crops were not submitted. This is acceptable for the representative use in pome fruits as this is a perennial crop.

As far as the use on ornamentals is concerned, fields used in this type of activity are normally not used in rotation with edible plant commodities. Nevertheless as no information has been submitted, a label restriction should be considered at Member State level, in case of possible conversion of a soil from ornamental to agricultural or horticultural production as well as in case of possible use of spent compost and growing media in ornamental production as fertilizer on agricultural areas.

[11] R1: 2-dodecyl-3-hydroxynaphthalene-1,4-dione.
[12] AKM-18: 2-(2-oxotetradecanoyl)benzoic acid.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Considering the potential exposure of livestock to acequinocyl residues through consumption of apple pomace (which was assessed to be lower than 0.1 mg/kg dry diet, even considering a potential transfer factor of 5 for apple pomace), no livestock metabolism study is in principle required and a residue definition for animal commodities is not necessary.

A metabolism study in lactating goats has however been submitted. The animal exposure was 2 orders of magnitude higher than the expected critical exposure. Total radioactive residues (TRR) in liver and kidneys were 0.14 and 0.10 mg/kg respectively, and below 0.02 mg/kg in other edible tissues and milk. This confirms that under practical condition, the transfer of acequinocyl to animal commodities will result in very low residue levels, well below the Limit of Quantification (LOQ) of usual methods of analysis.

The metabolic pattern was investigated in liver, kidney and fat, but not in muscle and milk. Parent compound and 3 metabolites were identified (R1, AKM-018 and AKM-15[13]) in amounts varying according to tissue.

3.3. CONSUMER RISK ASSESSMENT

Based on the calculations reported here below no risk for the consumer resulting from the use of acequinocyl according to the representative uses in apples and pears has been identified.

Chronic exposure.

The chronic dietary exposure assessment has been based on the Theoretical Maximum Daily intake (TMDI) calculation model of WHO using the WHO typical European diet for adult consumers and the Dutch national diet for adults and 1 to 6 year old children. Residues in apples and pears were considered to be at the level of proposed MRL (0.05 mg/kg). Based on these assumptions, the calculated TMDI was below 2 % of the ADI for the considered diets.

Acute exposure.

The acute exposure to residues of acequinocyl in apples and pears has been assessed according to the WHO model for conducting National Estimates of Short Term Intakes (NESTI) calculations. Large portion consumption data for adults and 1-6 year old children in The Netherland were used. Calculations were carried out considering residues of acequinocyl in composite samples of treated commodities at the level of the HR found in supervised trials. The unit to unit variability factor used was 5. Under these conditions none of the calculated NESTI exceeded 4 % of the ARfD.

3.4. PROPOSED MRLS

Based on the results of supervised residue trials and their analysis according to the statistical methods recommended by the current guidelines a MRL of 0.05 mg/kg in apples and pears is proposed reflecting the representative use supported by the applicant for these commodities.

[13] AKM-15: 6-(3-hydroxy-1,4-dioxo-1,4-dihydronaphthalen-2-yl)hexanoic acid

4. Environmental fate and behaviour

Acequinocyl was discussed at the PRAPeR experts' meeting for environmental fate and behaviour (PRAPeR 07) in November 2006.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation of acequinocyl in soil under dark aerobic conditions at 20 ºC (one soil at 10 ºC) was investigated in two studies with acequinocyl either ^{14}C-labelled at the phenyl ring (4 soils) or at the dodecyl moiety (2 soils). The soils covered a range of pH values (5.9–8.1), organic carbon content (0.6–4.6%) and clay content (2.82–33.1 %). In addition two soils were tested at the normal application rate and at high application rate to assure a proper determination of possible metabolites. The major metabolite in soil extracts was **R1**[14] (max. 33.8% AR after 2 days in the test with ^{14}C-phenyl acequinocyl applied at normal rate), formed by hydrolysis of the parent molecule. A second major metabolite was **AKM-18**[15] (max. 21.9% AR after 2 days in the second test with ^{14}C-phenyl acequinocyl), formed by the oxidation of R1. It is assumed that the microbial action plays an important role in the degradation of acequinocyl, since R1 and AKM-18 were formed much more slowly in sterile soil, in which CO_2 was not formed at all. In the non-sterile soils CO_2 was formed at a maximum of 15.0 – 57.7% AR at study end (120/180d). The formation of residues not extracted with acetonitrile/water was also a significant sink for the applied radioactivity (25.1-46.3% AR after 120/180 days at 20 ºC and up to 55.9% AR at 10 ºC), with most of the radioactivity associated to the immobile fractions (humin fraction and humic acids).

In an anaerobic soil degradation study with [^{14}C-phenyl] acequinocyl, the same major metabolites identified in the aerobic studies were formed; i.e. R1 (maximum 41.1% AR after 14 days) and AKM-18 (13.8% AR after 138 days).

According to the available study, photolysis may contribute to the dissipation of acequinocyl in soil. AKM-18 (maximum 23.7% AR after 6 days) and the unknown **Metabolite A** (maximum 13.8% AR after 2 days and identical to the minor metabolite A of the aerobic soil study) were determined as major metabolites in irradiated soil. In non-irradiated soil, a total of ten radioactive fractions were determined with R1, AKM-18 and Metabolite A as major (> 10% AR) metabolites.

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Sufficient information on persistence of acequinocyl in soil is available. However, only in some cases (4 soils) the available data in the laboratory metabolism studies were appropriate for kinetic calculations of degradation rates of the major metabolites R1 and AKM-18. Acequinocyl exhibited low persistence in soil with first order DT_{50}lab values at 20ºC in the range of 1.1-2.7 days. Degradation of the major metabolite AKM-18 is also fast (DT_{50}lab at 20ºC = 3.5 days). The major

[14] R1: 2-dodecyl-3-hydroxynaphthalene-1,4-dione
[15] AKM-18: 2-(2-oxotetradecanoyl)benzoic acid

metabolite R1 exhibited low to moderate persistent in soil with the DT_{50}lab at 20ºC ranging from 2 to 33 days.

Field dissipation of acequinocyl and its metabolites R1 (acequinocyl-OH) and AKM-18 (a benzoic acid) was studied over a period of 240 days at three sites in the United States. Following two applications at a nominal application rate of 0.336 kg a.s./ha with an interval of 21 days, acequinocyl declined rapidly with time. The AKM-18 metabolite was only incidentally found. Residues declined to < LOQ for all analytes within 15-72 hours. No residues were found below 15 cm. First order DT_{50} as recalculated by RMS were in the range of 2.2-6.2 hours (DT_{90} = 7.3-20.6 hours) for acequinocyl and 2.8-7.2 hours for metabolite R1 (DT_{90} = 9.1-23.9 hours).

PECsoil values for acequinocyl and its metabolites R1 and AKM-18 were recalculated with worst case laboratory DT_{50} values (addendum October 2006) and accepted by the experts of PRAPeR 07.

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The parent compound acequinocyl and its major metabolites R1 and AKM-18 can all be classified as immobile in soil. In three different types of soil, reliable adsorption K_{oc} values of acequinocyl varied between 33900 and 123000 L/kg. Freundlich coefficients and isotherms could not be obtained due to the limited water solubility of acequinocyl. The adsorption/desorption of metabolite R1 was investigated in four soils. Three calculated adsorption Kf_{OC} values were considered acceptable and varied from 9000 and 230000 L/kg (1/n = 0.72-1.0), indicating that metabolite R1 is immobile in soil. Indicative adsorption coefficients of metabolite AKM-18 are available for three soils, showing that also AKM-18 is immobile in soil (Kf_{OC} = 9698-52750 L/kg; 1/n = 1.30-1.62). There was no indication that adsorption of either acequinocyl or its metabolites were pH dependant based on the available information.

The leaching behaviour of acequinocyl and its aged residues was studied in a soil column leaching study. The test was performed with four soils. In both “unaged” and “aged” column leaching tests, the major part of the radioactivity remained in the top section of the soil columns. In the unaged leaching test > 74% total residues/radioactivity were retained in the top 10 cm. Apart from acequinocyl which accounted for 26.3-44.7% AR, various metabolites could be determined. Between 0.1-0.7% AR was determined in the leachates, with the exception of the leachate form the sand column in which 4.0% AR was determined. Neither acequinocyl nor R1 or AKM-18 was determined in this leachate. In the aged leaching test most of the radioactivity (73.6-79.4% AR) remained in the top section of the column and very little radioactivity (0.6-0.9% AR) were detected in the leachate.

It is concluded that acequinocyl and its major metabolites have a very low potential for leaching in soil.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Hydrolysis studies were carried out at two temperatures (15 and 25ºC) in different aqueous solutions buffered at pH values of 1.2, 4, 7 and 9. Hydrolysis increased in the order of pH 4 < pH 7 < pH 9.

Under acidic conditions the hydrolysis is slower, with an estimated DT_{50} of 74 days at 25ºC, respect to hydrolytic degradation at pH 7 (DT_{50} of 52 hours at 25ºC) and pH 9 (DT_{50} of 67 minutes at 25ºC).
The most significant hydrolysis product was R1 (max 55% AR, after 96 hours at pH 7 and 25 ºC). Another metabolite (max 11% AR at any pH value in the test at 15°C and 16.9% AR at pH 7 at 25°C) was identified as AKM-18[16]. This metabolite is most likely formed by oxidative processes and has also been identified in aerobic soil and in the water/sediment study.
In the DAR, a photolysis study performed with unlabelled acequinocyl was available but considered unacceptable. A second study performed with [^{14}C-phenyl] acequinocyl was presented in an addendum (October 2006) and accepted by the experts of PRAPeR 07. As a result of exposure to light, acequinocyl is degraded by direct photolysis with a DT_{50} of 14 minutes in the sterilised buffer system at pH 5. In the dark control the estimated half-life was 16 days. The major degradation products of photolysis were AKM-08[17] (max 13% AR after 120 minutes irradiation in the buffer system) and o-phthalic acid (max 12.7% AR in buffer system at the end of the study). Similar results were observed in the river water system (pH 7.8), with an estimated DT_{50} value of 12 minutes in the irradiated samples.
A ready biodegradability CO_2 evolution test indicated that acequinocyl is considered “not readily biodegradable”.
An aerobic water/sediment study using [^{14}C-phenyl] labelled acequinocyl was conducted at 20ºC in two systems. Acequinocyl disappeared very rapidly from the water phase and the major part of the radioactivity was recovered in the sediment as non extractable residues (max 59.7-62.0% AR after 30-60 days). In the water phases a total of seven radioactive fractions were characterised. Only R1 (max 12% AR at 0d only in the clay system) and **CBAA**[18] (max 7.9-11.3% AR after 2-14 days) were identified as major metabolites. In the sediment, the concentration of acequinocyl reached 8.4-26.4% AR at day 0.25-1, and AKM-18 was the only major metabolite (max 12.1-15.3% AR after 1 or 7 days). First order DT_{50} and DT_{90} values for the whole systems (water and sediment) were recalculated by RMS and resulted to be < 0.5 days and < 1.6 days, respectively. Due to the limited amount of data > LOQ in the study, no reliable kinetic analysis was possible for degradation of acequinocyl and its metabolite in the water phase. However, estimations were performed with the measured concentrations at successive time intervals, resulting in $DT_{50water}$ < 1d and $DT_{90water}$ < 2d.
The submission of acequinocyl dossier for authorisation was received by RMS prior to FOCUS surface water modelling being required, therefore predicted environmental concentrations (PEC) in surface water were calculated for the spray drift route of entry assuming single first order $DT_{50water}$ of <0.75 days. The contribution from drainage and run-off was not assessed and may need to be taken into account by MS for those situations where these routes of surface water contamination are envisaged to be relevant. For the metabolites R1 and CBAA only initial concentrations, based on the maximum amounts observed in the water phase of the water/sediment studies, were estimated to be used in a first tier risk assessment for aquatic organisms. It should be noted that some of the calculated PECsw for acequinocyl exceed the very low solubility of the active substance in pure

[16] AKM-18: 2-(2-oxotetradecanoyl)benzoic acid
[17] AKM-08: 2-hydroxy-3-(2-oxoheptyl)naphthalene-1,4-dione
[18] CBAA: 2-(carboxycarbonyl)benzoic acid

water (6.7 µg/L at 25ºC). The experts of PRAPeR meeting 07 agreed that PECsediment calculations are not necessary as the risk assessment for both the parent and the metabolite AKM-18 were based on a spiked water sediment dweller test and for a GAP with only one application per year for outdoor uses.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Groundwater modelling was available using FOCUS PEARL model and scenarios for the applied for intended uses of apple and ornamentals. Since FOCUS PEARL has no standard scenario for ornamentals, scenarios for strawberries, vines and sunflowers were selected. Simulations were performed for a single application of 281 g a.s./ha on apples and for a single application of 600 g a.s./ha on ornamentals on May 1st (early application) and September 1st (late application). PECgw values for the soil major metabolites R1 and AKM-18 were calculated assuming that the metabolites are formed at a maximum of respectively 33.8% and 21.9% of the applied dose. The predicted annual average concentrations of acequinocyl and its metabolites R1 and AKM-18 in leachate leaving the top 1 m soil column were estimated to be < 0.001 µg/L at all scenarios (significantly less than the parametric drinking water limit of 0.1 µg/L).

4.3. FATE AND BEHAVIOUR IN AIR

A theoretical calculation of the photo-oxidation of acequinocyl in the atmosphere, using the method of Atkinson gave a DT_{50} of 1.21 hours, assuming 12 hour light per day, suggesting that the concentrations of acequinocyl in air are negligible.

5. Ecotoxicology

Acequinocyl was discussed at the PRAPeR experts' meeting for ecotoxicology (PRAPeR 08) in November 2006.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The representative uses of acequinocyl evaluated are the uses as an acaricide in ornamentals and apple/pear orchards. The acute and short-term TERs in the first tier risk assessment were above the Annex VI trigger of 10 for insectivorous and herbivorous birds as well as the acute TER for herbivorous mammals. A revised refined long-term risk assessment was presented in the addendum and discussed in the expert meeting. It was suggested to refine the NOEC by taking the geometric mean value of two available studies. However concerns were raised by the experts that some taxonomic groups of birds could be particularly sensitive. It was also pointed out that in the past always the lowest endpoint from available studies was used in the risk assessment and that taking the geometric mean value would lower the level of protection in comparison with previous risk assessments. Therefore the meeting agreed to take the lowest NOEL of 7.48 mg acequinocyl/kg bw/d. It was not possible to derive a robust DT_{50} for residue decline in insects but the experts agreed that

there is enough information to conclude that the DT_{50} will be less than 3 days. The recalculation of the DT_{50} of foliar residue decline of 9.1 days was based on studies with application to apple leaves. Extrapolation to residue decline in grass or herbs was not considered as scientifically robust enough and the experts suggested using the default value of 10 days for the risk assessment. The corresponding long-term TERs are >4.3 (orchard) and >2 (ornamentals) for insectivorous birds and 0.76 (ornamentals) for herbivorous birds. The risk to insectivorous birds in orchards was considered as low since the long-term TER of >4.3 is based on a greater than value (due to residue decline in insects).

The relevance of ornamentals as a food source for herbivorous birds was discussed in the meeting. No conclusion was reached due to the lack of further information. A data gap was identified for further refinement of the long-term risk assessment for insectivorous and herbivorous birds for the use in ornamentals grown in fields.

The long-term risk assessment for herbivorous mammals was based on a refined long-term NOAEL of 6.9 mg/kg bw/d. The proposal to reduce the PT value to 0.5 and 0.1, respectively was not supported by any data and hence rejected. The long-term TERs are 0.69 and 1.73 for the use in orchards and ornamentals. Further refinement of the long-term risk assessment of herbivorous mammals is necessary.

The first-tier risk assessment for earthworm-eating birds and mammals resulted in TERs below the trigger of 5. The refined risk assessment was based on an experimentally derived BCF for earthworms. It was noted during the expert-meeting that the BCF of 22.1 was based on worm dry weight instead of wet-weight. The corrected value of 1.86 was used in the TER calculations in the updated addendum from September 2007 (not-peer reviewed). The TERs were above the trigger of 5 for the use in orchards and in ornamentals indicating a low risk for earthworm-eating birds and mammals.

The risk from secondary poisoning of fish-eating birds and mammals was assessed as low.
No major plant metabolites were found in the residue studies and hence the risk from plant metabolites to herbivorous birds and mammals is considered as low.

Overall it is concluded that the long-term risk assessments for insectivorous and herbivorous birds and herbivorous mammals need further refinement. The RMS confirmed that new risk assessments were submitted in May 2007.

5.2. RISK TO AQUATIC ORGANISMS

Crustaceans were the most sensitive group of aquatic organisms tested. The lowest acute endpoints were observed for *Daphnia magna* (3.9 µg acequinocyl/L) and *Mysidopsis bahia* (0.93 µg acequinocyl/L). A study with 8 freshwater invertebrate species was submitted by the applicant. The

experts recommended not to use the study in the risk assessment since sediment was added to the test system and hence the a.s. rapidly removed from the water phase.
A revised aquatic risk assessment based on a microcosm study was submitted and evaluated in an addendum. The experts in the meeting agreed that the NOEC(population) of 3 µg acequinocyl/L should be used in the risk assessment. Concerns were raised that the endpoint would not cover the risk to sensitive crustacean species such as mysids and a safety factor of 3-5 was proposed by the experts. The TER calculation was based on entry into surface water via spray drift only (see section on fate and behaviour point 4.2.1). Risk mitigation measures such as no-spray buffer zones of 30 m (orchards late application and ornamentals >50 cm high) and 10 m (ornamentals <50 cm high) are required to achieve TERs of >5. In order to reach a TER >3 for the early use in orchards a no spray buffer zone of 30 m is required and the buffer zone needs to be extended to 50 m to achieve a TER of >5. The RMS confirmed that additional studies with crustaceans were submitted by the applicant in April 2007.

The major metabolites in the water phase (R1 and CBAA) were tested with fish indicating a low toxicity. No studies were conducted with invertebrates or algae. However it is likely that the metabolites were formed in the microcosm and hence the risk from these metabolites to invertebrates and algae is covered by the risk assessment based on the microcosm endpoint.

The risk to sediment dwelling organisms was assessed as low based on a study with *Chironomus riparius*. AKM-18 is a major metabolite in the sediment phase. The metabolite was not measured in the test system and the formation rate in artificial sediment is uncertain. However considering that the metabolite was rapidly formed and reached its peak concentrations at days 1-7 in the water-sediment study it is likely that the metabolite was present in the 29 d static study with *C. riparius*. Hence the risk from the metabolite AKM-18 to sediment dwelling organisms is considered to be covered by the risk assessment for the parent.

5.3. RISK TO BEES

Acute oral and contact toxicity studies were conducted with technical and formulated acequinocyl. The HQ values were below the Annex VI trigger of 50 indicating a low risk to bees from the representative uses evaluated.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory tests were conducted with acequinocyl formulated as AKD-2023 15% SC and the arthropod species *Aphidius rhopalosiphi, Typhlodromus pyri, Poecilus cupreus, Pardosa sp, Aleochara bilineata, Amblyseius andersoni,* and *Phytoseiulus persimilis.* No effects of >30% were observed at the rates of 300, 600, 624 and 1050 g a.s./ha applied in the tests except in one study with *P. persimilis*. New aged residue studies with *T. pyri* and *P. persimilis* were submitted and evaluated by the RMS in the addendum. No effects of >50% were observed when the animals were exposed to fresh residues on natural substrate at application rates of 1800 g a.s./ha. The magnitude of adverse effects on *P. persimilis* was not reduced after several days of ageing of residues. This effect was

explained by reduction of availability of prey (mite eggs). The risk assessment was agreed in the expert meeting and it was concluded that the risk to non-target arthropods is low from the representative uses evaluated.

5.5. RISK TO EARTHWORMS

The acute toxicity to earthworms was tested with technical acequinocyl and formulated as AKD-2023 15% SC. Acequinocyl if is of low toxicity to earthworms. The 14-d LC_{50} of > 1000 mg a.s./kg was corrected by a factor of 2 since the log P_{ow} is >2. The acute TERs were >6667, >1250 and >1035 for the use in orchards, ornamentals (field) and ornamentals (glasshouse) indicating a low risk.

Chronic testing was considered not necessary because the field DT_{90} of acequinocyl in soil is less than 100 days. The major soil metabolites R1 and AKM-18 are formed rapidly. One of the studies with earthworms was conducted with natural soil. The metabolites reached the peak concentrations in the degradation studies within 2-10 days. Therefore it is likely that the metabolites were formed in the test with natural soil (duration of 14 days) and that the risk from the metabolites is considered to be covered by the available risk assessment.

5.6. RISK TO OTHER SOIL NON-TARGET MACRO-ORGANISMS

No studies required since the field DT_{90} of acequinocyl in soil is <100 d.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No effects of >25 % on soil respiration and nitrification were observed in tests with technical acequinocyl up to concentration of 7 mg a.s./kg soil dw (equivalent to an application rate of about 5 times the proposed field application rate) indicating a low risk to soil non-target micro-organisms for the representative uses evaluated. Some replicates were removed from the analysis of the soil respiration test. Further information was submitted and evaluated by the RMS in the addendum confirming that it was correct not to include the outliers in the calculations. The soil respiration and nitrification test has been conducted with natural soil. Therefore it is likely that the major soil metabolites R1 and AKM-18 were formed during the test period of 29 days and potential effects of the metabolites on soil respiration and nitrification were covered by the available test.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

Herbicidal effects of the formulation AKD-2023 15% SC on vegetative vigour and emergence were investigated in tests with 6 dicotyledon plant species and with 4 monocotyledon plant species. No statistically significant effects and no clear dose-response relationships were observed at the tested application rates of 5 and 15 kg formulation/ha (more than 3 times the maximum application rate). The risk to non-target plants in the off-field area is considered to be low for the representative uses evaluated.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Technical acequinocyl did not inhibit the respiration of activated sewage sludge at concentrations of 1 – 1000 mg a.s./L. Undissolved acequinocyl was observed at the highest tested concentrations of 100 and 1000 mg a.s./L. In the meeting of experts it was agreed that this does not invalidate the test. No adverse effects were observed up to the threshold of solubility and it was agreed that the risk to biological sewage treatment is low if the product is applied according to the GAP.

6. Residue definitions

Soil

Definition for risk assessment: acequinocyl, R1[19], AKM-18[20]

Definition for monitoring: acequinocyl

Water

Ground water

Definition for exposure assessment: acequinocyl, R1, AKM-18

Definition for monitoring: acequinocyl (in the case of accident or spillage of acequinocyl, as $DT_{90water}$ < 2 days, metabolite R1 may be a more appropriate indicator)

Surface water

Definition for risk assessment: acequinocyl (water and sediment), R1 (water), CBAA[21] (water), AKM-18 (sediment)

Definition for monitoring: acequinocyl (in the case of accident or spillage of acequinocyl, as $DT_{90water}$ < 2 days, metabolite CBAA may be a more appropriate indicator; however, as the analytical method for this metabolite is not validated, metabolite R1 can be used as a substitute indicator)

Air

Definition for risk assessment: acequinocyl

Definition for monitoring: acequinocyl

Food of plant origin

Definition for risk assessment: acequinocyl.

Definition for monitoring: acequinocyl.

Food of animal origin

Definition for risk assessment: not necessary considering that livestock exposure is very low.

Definition for monitoring: not necessary considering that livestock exposure is very low.

[19] R1: 2-dodecyl-3-hydroxynaphthalene-1,4-dione
[20] AKM-18: 2-(2-oxotetradecanoyl)benzoic acid
[21] CBAA: 2-(carboxycarbonyl)benzoic acid

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
acequinocyl	Very low to low persistent 1st order DT_{50lab} = 1.1 – 2.7 d (20ºC and 40% MWHC)	Low toxicity and low risk to earthworms and soil micro-organisms
R1	Low to moderate persistent 1st order DT_{50lab} = 2.0 – 33 d (20ºC and 40% MWHC)	No tests available. Potential adverse effects on earthworms and soil micro-organisms are covered by the risk assessment for acequinocyl.
AKM-18	Low persistent 1st order DT_{50lab} = 3.5 d (20ºC and 40% MWHC)	No tests available. Potential adverse effects on earthworms and soil micro-organisms are covered by the risk assessment for acequinocyl.

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
acequinocyl	Immobile (K_{oc} = 39900 – 123000 L/kg)	No	Yes	Yes	Yes
R1	Immobile (Kf_{oc} = 9000 – 230000 L/kg)	No	No data available No data required	Low acute oral and dermal toxicity Unlikely to be genotoxic	No data available No data required

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
AKM-18	Immobile (Kf_{oc} = 9697 – 52750 L/kg)	No	No data available No data required	Low acute oral toxicity Unlikely to be genotoxic	No data available No data required

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
acequinocyl (water and sediment)	See point 5.2.
R1 (water)	Low toxicity and risk to fish. No studies conducted with invertebrates or algae. However the risk assessment covers potential adverse effects on algae and invetebrates which based on a mesocosm endpoint.
CBAA (water)	Low toxicity and risk to fish. No studies conducted with invertebrates or algae. However the risk assessment covers potential adverse effects on algae and invetebrates which based on a mesocosm endpoint.
AKM-18 (sediment)	No test with AKM-18 is available. However it is likely that the metabolite was formed in the test with acequinocyl and *Chironomus riparius* and hence the risk is considered to be covered by the endpoint derived in the test.

Air

Compound (name and/or code)	Toxicology
acequinocyl	LC_{50} inhalation, rat (4-hour, whole body exposure) > 0.84 mg/L, no classification is proposed.

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

- A data gap was identified for a new technical material specification (relevant for all representative uses evaluated; already submitted, presented in addendum to Vol.4, not peer reviewed, refer to chapter 1).
- The long-term risk assessment for insectivorous and herbivorous birds needs refinement (relevant for the field use in ornamentals; the applicant submitted a new risk assessment to the RMS in April 2007; refer to point 5.1).
- The long-term risk assessment for herbivorous mammals needs refinement (relevant for the use in orchards and the field use in ornamentals; the applicant submitted a new risk assessment to the RMS in April 2007; refer to point 5.1).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as proposed by the applicant which comprise field and greenhouse foliar spraying to control *Tetranychus urticae* in ornamentals, up to a maximum one treatment in outdoor use, and maximum 3 treatments in greenhouses, at a maximum application rate per spray of 150-600 g as/ha at a 7 day interval between applications in greenhouses and also foliar spraying to control *Panonychus ulmi* in apples and pears up to a maximum one treatment, at a maximum application rate per spray of 150-280 g as/ha.

The representative formulated product for the evaluation was “Kanemite”, a suspension concentrate (SC) containing 164 g/L acequinocyl, provisionally registered in Austria and Germany as Kanemite and in the Netherlands as Cantack.

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

Regarding the mammalian metabolism, there are distinct indications for sizeable biliary first pass elimination. However, based on the critical effect of acequinocyl, the extent of oral absorption was considered to represent 28% of the administered dose. Excretion occurs predominantly via bile/faeces and no potential for accumulation was seen. Acequinocyl is extensively metabolized with 0-2.5% parent compound found in urine, bile or faeces.
Acequinocyl has low acute toxicity and is not a skin or eye irritant; however classification is required for skin sensitization based on a Maximisation test. In repeated dose studies, acequinocyl caused haematological effects (increased platelet levels and blood clotting time) in rats, mice and dogs; in

addition, ocular effects were observed in the rats and hepatotoxicity in mice. No genotoxic or carcinogenic potential was observed. Acequinocyl showed no effect on fertility parameters and produced effects on the reproductive or developmental parameters in rats or rabbits only at parental toxic doses. No potential for neurotoxicity was evidenced. Four acute studies in rats and monkey were submitted to investigate the effects of acequinocyl on the blood clotting system resulting in an overall NOAEL of 8 mg/kg bw for prolongation of blood clotting time in rats.

The acceptable daily intake (ADI) is set at 0.023 mg/kg bw/day and the acute reference dose (ARfD) at 0.08 mg/kg bw considering an assessment factor of 100; the acceptable operator exposure level (AOEL) is set at 0.014 mg/kg bw/day considering an assessment factor of 357 (correction of 28% for oral absorption). Dermal absorption is 3.6% when handling the concentrate formulation and 16.7% when handling the spray dilution. Considering the representative uses of Kanemite SC outdoor (apple/pear and ornamentals), the estimated operator exposure exceeds the AOEL according to the UK POEM model; according to the German model calculations, exposure is below the AOEL only when the use of PPE as protective gloves during mixing/loading and gloves, protective garment and sturdy footwear during application is considered. According to the Dutch model for greenhouse applications (ornamentals), the exposure of operators was calculated to represent twice the AOEL (210%) when using a default reduction factor of 10% for the use of PPE. Worker exposure after outdoor applications on apple and pear (mechanical upward spraying) is estimated to be below the AOEL even without the use of PPE, but for downward application on ornamentals, outdoor and in greenhouses, the use of gloves is required to obtain a level of exposure lower than the AOEL. Exposure of bystanders is estimated to be below the AOEL.

The metabolism of acequinocyl in fruit crops is clearly elucidated. For PHIs up to 30 days, the parent compound is the major constituent of the residue and no metabolite was found in amounts suggesting a significant contribution to the toxicological burden. The residue definition for monitoring and risk assessment can therefore be restricted to acequinocyl. Supervised residue trials were performed in Northern and Southern Europe and form a sufficient basis for proposing an MRL to be set at 0.05 mg/kg in apples and pears.

Considering this low residue level, no study on the effect of processing was estimated necessary.

No information has been provided on the potential transfer of soil residues to rotational or succeeding crops considering that cultivation of edible agricultural or horticultural crops in rotation with the representative uses does not normally occurs in practice. In case this should be possible practice at national level, Member States should consider the opportunity of label restriction.

A metabolism study in lactating goat was submitted although not required given that livestock exposure through consumption of apple pomace is extremely low. This study was considered but not used for proposing a residue definition.

Consumer chronic and acute exposures are well below the toxicological reference values and no dietary risk is expected resulting from the use of acequinocyl following the supported representative uses.

Sufficient data were available to satisfy the data requirements and characterise the fate and behaviour of acequinocyl in the environment as required by the current regulatory framework. The drainage and runoff routes of exposure to surface water have not been covered for acequinocyl and its metabolites R1 and CBAA in the available EU level assessment. This exposure assessment and the associated risk assessment to aquatic organisms should be completed in national assessments made by Member States where deemed appropriate. For the applied for intended uses, the potential for groundwater exposure by acequinocyl and its major metabolites R1 and AKM 18 above the parametric drinking water limit of 0.1 µg/L, is low.

The acute and short-term risk to birds and the acute risk to mammals was assessed as low in the first-tier risk assessment. A refined long-term risk assessment for birds and mammals was required. The suggested refinement steps were rejected in the experts meeting. The long-term TER of 4.3 for insectivorous birds in orchards was below the trigger of 5 but considered as sufficient to conclude on a low risk since the available information on residue decline in insects suggest a rapid decline with a DT_{50} of <3 days. A data gap was identified to refine the long-term risk to herbivorous and insectivorous birds for the use in ornamentals. The PT values proposed to refine the long-term risk to mammals were rejected because no supporting data were made available.

Acequinocyl is very toxic to aquatic invertebrates. In the meeting of experts it was agreed that the aquatic risk assessment should be based on the NOEC (population effects) of 3 µg acequinocyl/L derived from a microcosm study in combination with an assessment factor of 3-5. No spray buffer zones of 30 m (orchards late application and ornamentals >50 cm high) and 10 m (ornamentals <50 cm high) are required to achieve TERs of >5. In order to reach a TER of >3 for the early use in orchards a no spray buffer zone of 30 m is required and the buffer zone needs to be extended to 50 m to achieve a TER of >5.

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

Particular conditions proposed to be taken into account to manage the risk(s) identified

- Operator exposure for outdoor applications is estimated to be below the AOEL only if PPE as protective gloves are used during mixing/loading and gloves, protective garment and sturdy footwear are used during application, according to the German model (refer to point 2.12).
- Re-entry exposure after ornamentals application (outdoor and in greenhouses) is estimated to be below the AOEL only if PPE as protective gloves are used (refer to point 2.12).
- It is proposed to use a NOEC of 3 µg acequinocyl/L derived from a microcosm study and an assessment factor of 3-5 in the aquatic risk assessment. Risk mitigation measures such as no-spray buffer zones of 30 m (orchards late application and ornamentals >50 cm high) and 10 m (ornamentals <50 cm high) are required to achieve TERs of >5. In order to reach a TER of >3 for the early use in orchards a no-spray buffer zone of 30 m is required and the buffer zone needs to be extended to 50 m to achieve a TER of >5.

Critical areas of concern

- Operator exposure for greenhouse application, considering mixing, loading and application exposure, exceeds the AOEL even when the use of PPE is considered.
- A high long-term risk to birds and mammals
- A high risk for aquatic organisms for the use in orchards and ornamentals (>50 cm high).

APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

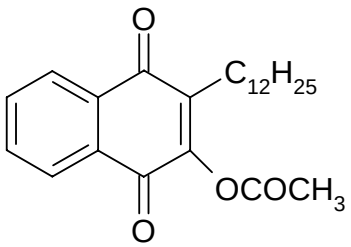
(Abbreviations used in this list are explained in appendix 2)

Appendix 1.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Acequinocyl
Function (e.g. fungicide)	Acaricide

Rapporteur Member State	The Netherlands
Co-rapporteur Member State	None

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	3-dodecyl-1,4-dihydro-1,4-dioxo-2-naphthyl acetate
Chemical name (CA) ‡	2-(acetyloxy)-3-dodecyl-1,4-naphtalenedione
CIPAC No ‡	760
CAS No ‡	57960-19-7
EC No (EINECS or ELINCS) ‡	None
FAO Specification (including year of publication) ‡	Not established
Minimum purity of the active substance as manufactured ‡	Minimum 96%
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	No relevant impurities
Molecular formula ‡	$C_{24}H_{32}O_4$
Molecular mass ‡	384.5 g/mol
Structural formula ‡	

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	59.6 °C (99.5%)
Boiling point (state purity) ‡	It was concluded that the substance has no boiling point below 200°C, as decomposition takes place above 200°C.
Temperature of decomposition (state purity)	At 200°C the test substance changed colour to brown and to black at 300°C. No bubbles where visible. It was concluded that the substance has no boiling point below 200°C, as decomposition takes place above 200°C
Appearance (state purity) ‡	Light brown flakes (98.25%) Soft yellow crystals (99.9%)
Vapour pressure (state temperature, state purity) ‡	1.69×10^{-6} Pa (25°C)
Henry's law constant ‡	9.7×10^{-2} Pa.m^3/mol
Solubility in water (state temperature, state purity and pH) ‡	6.69×10^{-6} g/L (25°C) Not pH dependent
Solubility in organic solvents ‡ (state temperature, state purity)	Solvent — Solubility g/L (20°C) methanol — 6.1 acetone — > 250 n-heptane — 36.0 1-octanol — 29.2 1,2-dichloroethane — > 250 ethyl acetate — > 250 xylene — >250
Surface tension ‡ (state concentration and temperature, state purity)	Not determined (solubility in water is < 1 mg/L)
Partition co-efficient ‡ (state temperature, pH and purity)	Log Kow > 6.2 (25°C) Not pH dependent
Dissociation constant (state purity) ‡	No dissociation, at least within the range of pH 3 - 10

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)		λmax (nm)	ε (L.mol^{-1}.cm^{-1})
	Acidic (0.1 M HCL in methanol/ water 90/10)	242	16524
		248	16989
		270	13905
		335	2836
	Neutral (methanol/ water 90/10)	242	16582
		248	16873
		270	13207
		271	2851
	Basic (0.1 M NaOH in methanol/water 90/10)	232	19055
		245	13149
		275	2172
		362	8999
Flammability ‡ (state purity)	Not highly flammable		
Explosive properties ‡ (state purity)	No explosive properties		
Oxidising properties ‡ (state purity)	Non-oxidising		

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Summary of representative uses evaluated *

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	g as/ha min – max (l)		
Ornamentals	NL, DE, FR, DK, BE	KANEMITE	G	*Tetranychus urticae*	SC	164	spraying	Not specified	1-3	7 d	15-30	1000-2000	150-600	n.a.	[1]
Ornamentals	NL, DE, FR, DK, BE	KANEMITE	F	*Tetranychus urticae*	SC	164	spraying	Not specified	1		15-30	1000-2000	150-600	n.a.	[2]
Apple/Pear	NL, DE, FR, DK, BE, IT, ES, GR, UK, AU, PT	KANEMITE	F	*Panonychus ulmi*	SC	164	spraying	Not specified	1		15-19	1000-1500	150-281	30	[2]

[1] Operator exposure exceeds the AOEL even when the use of PPE is considered.
[2] The long-term risk assessment for birds and mammals needs further refinement. Risk mitigation measures such as no-spray buffer zones of >30m are required for the use in orchards and ornamentals higher than 50cm.

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

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.2: Methods of Analysis

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

Technical as (analytical technique)	Reversed Phase-HPLC UV (235 nm)
Impurities in technical as (analytical technique)	Reversed Phase-HPLC UV (235 nm)
Plant protection product (analytical technique)	Reversed Phase-HPLC UV (235 nm)

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Acequinocyl
Food of animal origin		Not necessary considering that livestock exposure is very low
Soil		Acequinocyl
Water	surface	Acequinocyl
	drinking/ground	Acequinocyl
Air		Acequinocyl

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	LC/MS/MS; LOQ: 0.01 mg/kg (acequinocyl and metabolite R1 separately, apples, oranges, egg plant, grapes) *ILV required*
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	No method for animal products is required as no MRL is set
Soil (analytical technique and LOQ)	HPLC-MS/MS, LOQ: 0.01 mg/kg (acequinocyl and metabolites R1 and AKD-18 individually)
Water (analytical technique and LOQ)	HPLC-MS/MS, LOQ: 0.1 µg/L (acequinocyl and metabolite R1 individually, in surface, drinking and ground water) *Validated method for CBAA in surface water is required.*
Air (analytical technique and LOQ)	HPLC-MS/MS, LOQ: 0.075 mg/m^3 (acequinocyl and metabolite R1 individually)
Body fluids and tissues (analytical technique and LOQ)	Not relevant, acequinocyl is not a toxic compound.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

	RMS/peer review proposal
Active substance	No classification is proposed

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	At least 28%, after low dose, 48h after administration, based on radiolabel recovered from urine, bile, cage wash and carcass (rat). At least 4.8%, after high dose, 48h after administration, based on radiolabel recovered from urine, bile, cage wash and carcass (rat).
Distribution ‡	24 hours after single oral low dose (10 mg/kg bw), highest concentrations GI-tract and its contents; intermediate concentrations were in fat, kidneys, liver, lungs, lymph nodes and pancreas.
Potential for accumulation ‡	No evidence of accumulation.
Rate and extent of excretion ‡	Within 24h ca. 75% of low dose excreted and ca. 40% of high dose; within 120h ca. 95% excreted, mainly via faeces (ca. 87% after low dose).
Metabolism in animals ‡	Extensively metabolised (no parent compound in urine, 2% parent compound of total radiolabel in faeces and 2.5% of total radiolabel in bile).
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound
Toxicologically relevant compounds ‡ (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw	
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 0.84 mg/L (aerosol, 4h exposure, nose only)	
Skin irritation ‡	Not irritating	
Eye irritation ‡	Not irritating	
Skin sensitisation ‡	Sensitising (Maximisation test)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Blood	
Relevant oral NOAEL ‡	5 mg/kg bw/day (1-year, dog)	
Relevant dermal NOAEL ‡	200 mg/kg bw/day (28-day, rat)	
Relevant inhalation NOAEL ‡	No data – not required	

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Genotoxicity ‡ (Annex IIA, point 5.4)

……..	No genotoxic potential	

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

Target/critical effect ‡	Blood and eyes (rat), liver (mice)	
Relevant NOAEL ‡	2.3 mg/kg bw/day (2-year, rat) 2.7 mg/kg bw/day (80-week, mouse)	
Carcinogenicity ‡	No carcinogenic potential	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parent: haemorrhages and protruding eyes. Offspring: haemorrhagic effects, delayed physical and functional development before weaning at parental toxic doses. No reproductive effects.	
Relevant parental NOAEL ‡	6.9 mg/kg bw/day	
Relevant reproductive NOAEL ‡	>107 mg/kg bw/day	
Relevant offspring NOAEL ‡	6.9 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Maternal: haemorrhagic effects. Developmental: Increased incidence of 13th rib at maternal toxic doses. No teratogenic effects.	
Relevant maternal NOAEL ‡	150 mg/kg bw/day (rat) 60 mg/kg bw/day (rabbit)	
Relevant developmental NOAEL ‡	500 mg/kg bw/day (rat) 60 mg/kg bw/day (rabbit)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data – not required	
Repeated neurotoxicity ‡	No data – not required	
Delayed neurotoxicity ‡	No data – not required	

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Single oral administration of acequinocyl in doses ranging from 20 to 600 mg/kg bw to rats causes transient prolongation of blood clotting time (effects within 1 to 6 hours and ceased after 48 hours). An overall NOAEL for blood clotting effects of 8 mg/kg bw was established. Single oral administration of acequinocyl to rhesus monkeys in a dose of 1000 mg/kg bw seemed to produce minor increases in PT (prothrombin time) and PTT (partial thromboplastin time); no well founded conclusion possible.
Studies performed on metabolites or impurities ‡	Acute toxicity and genotoxicity studies were performed with metabolites AKM-18 and R1, which were not considered to be relevant metabolites. AKM-18: LD_{50} >5000 mg/kg bw (oral, mouse) Negative Ames test and negative in vitro chromosome aberration test. R1: LD_{50} >5000 mg/kg bw (oral, rat) LD_{50} >2000 mg/kg bw (dermal, rat) Negative in vivo micronucleus test (mouse bone marrow)

Medical data ‡ (Annex IIA, point 5.9)

……..	Limited, new active substance

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.023 mg/kg bw/day	2-year, rat	100
AOEL ‡	0.014 mg/kg bw/day	1-year, dog supported by 2-generation, rat	357*
ARfD ‡	0.08 mg/kg bw	mechanistic studies, single dose, rat	100

* Corrected by 28% oral absorption

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Dermal absorption ‡ (Annex IIIA, point 7.3)

Kanemite SC	3.6% (undiluted formulation) 16.7% (diluted formulation) based on *in vitro* (human, rat) and *in vivo* studies (rat) conducted with acequinocyl diluted in blank formulation

Exposure scenarios (Annex IIIA, point 7.2)

Operator	The estimated exposure for Kanemite SC according to the German model was below the AOEL, only if PPE are worn (gloves during m/l and application, protective garment and sturdy footwear during application). According to the UK POEM model, estimated exposure is above the AOEL even with PPE. Mechanical spraying on apple/pear (0.281 kg a.s./ha) German model: Without PPE: 465% of AOEL With PPE: 69% of AOEL (46% with additional PPE: broad-brimmed headgear) UK POEM Model: Without PPE: 645% of AOEL With PPE: 343% of AOEL Manual spraying on ornamentals outdoors (0.6 kg a.s./ha) German model: Without PPE: 886% of AOEL With PPE: 89% of AOEL (64% with additional PPE: broad-brimmed headgear) UK POEM Model: Without PPE: 786% of AOEL With PPE: 317% of AOEL Manual spraying on ornamentals indoors (0.6 kg a.s./ha); estimated with Dutch model Without PPE: 2102% of AOEL With PPE: 210% of AOEL

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Workers	The estimated exposure for Kanemite SC was below the AOEL with PPE (gloves) and for apple/pear also without PPE Re-entry activities in apple/pear, based on field studies and EUROPOEM II, re-entry at day 3 Without PPE: 31% of AOEL With PPE: 3% of AOEL Re-entry activities in apple/pear, based on field studies and EUROPOEM II, re-entry at day 0 Without PPE: 39% of AOEL With PPE: 4% of AOEL Re-entry activities in ornamentals outdoors, based on field studies and EUROPOEM II Without PPE: 500% of AOEL With PPE: 50% of AOEL Re-entry activities in ornamentals indoors, based on field studies and EUROPOEM II Without PPE: 500% of AOEL With PPE: 50% of AOEL
Bystanders	For both submitted outdoor uses (EUROPOEM II) and for indoor use no risk identified Apple/pear: 48% of AOEL Ornamentals outdoors: 10% of AOEL

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

	RMS/peer review proposal
Substance acequinocyl	Xi Irritant R43 May cause sensitisation by skin contact

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.4: Residues

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

Plant groups covered	Fruit crops (apples, orange, egg plant)
Rotational crops	Not applicable due to the intended use
Metabolism in rotational crops similar to metabolism in primary crops?	Not applicable (representative uses are perennial crops only)
Processed commodities	Not required (low residue levels in raw commodities)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not required
Plant residue definition for monitoring	Parent compound (acequinocyl, AKD-2023)
Plant residue definition for risk assessment	Parent compound (acequinocyl, AKD-2023)
Conversion factor (monitoring to risk assessment)	None

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

Animals covered	No study required One study on lactating ruminants available
Time needed to reach a plateau concentration in milk and eggs	Milk: not determined (above 5 days)
Animal residue definition for monitoring	Not required
Animal residue definition for risk assessment	Not required
Conversion factor (monitoring to risk assessment)	Not required
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes (in principle. However, no residues expected)

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

……..	To be evaluated at member state level depending on rotational practices of ornamentals at national level.

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

……..	Stable up to 18 months –18°C in apple fruit

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	No	No	No
Potential for accumulation (yes/no):	Not under livestock exposure resulting from representative uses	Not under livestock exposure resulting from representative uses	Not under livestock exposure resulting from representative uses
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	No
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	Not required	Not required	Not required
Liver	Not required	Not required	Not required
Kidney	Not required	Not required	Not required
Fat	Not required	Not required	Not required
Milk	Not required		
Eggs		Not required	

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
apples	Northern and Mediterranean Region	5 x < 0.01, 3 x 0.01, 1 x 0.012, 1 x 0.013, 2 x 0.014, 1 x 0.018, 1 x 0.025, 1 x 0.026, 1 x 0.030, 1 x 0.039, 1x 0.042	In most trials two treatments were applied instead of the single treatment as stated in the cGAP. The trials were used due to the fast decline of the residues in commodities in combination with the applied minimum period between the two applications - no significant contribution of the first application to the finally measured residue levels are expected at the intended PHI.	0.05 mg/kg	0.042 mg/kg	0.013 mg/kg

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

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

ADI	0.023 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	0.19
TMDI (% ADI) according to national (to be specified) diets	Dutch model for the whole population: 0.3% for children, age of 1 – 6 years: 1.5%
IEDI (WHO European Diet) (% ADI)	Calculation not necessary
NEDI (specify diet) (% ADI)	Calculation not necessary
Factors included in IEDI and NEDI	Calculation not necessary
ARfD	0.08 mg/kg bw
IESTI (% ARfD)	Only Dutch diet used for acute exposure assessment
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Dutch model for the whole population: 1.1% for children, age of 1 – 6 years: 3.5%
Factors included in IESTI and NESTI	HR, variability factor of 5, no processing factor

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
No processing studies are required, since human TMDI accounts for less than 10% of the ADI.				

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

apples	0.05 mg/kg
pears	0.05 mg/kg

* LOQ

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	39.2 – 57.7% a.r. after 120/180d [14C-Phenyl] label (n=4), normal application rate (0.5 mg/kg), 20°C 43.9 – 45.8% a.r. after 180d [14C-Dodecyl] label (n=2), normal application rate (0.5 mg/kg), 20°C 15.0 – 15.9% a.r. after 176/309d [14C-Phenyl] label (n=2), high application rate (20 mg/kg), 20°C 15.1% a.r. after 176d [14C-Dodecyl] label (n=2), high application rate (20 mg/kg), 20°C 26.6% a.r. after 120d [14C-Phenyl] label (n=1), normal application rate (0.5 mg/kg), 10°C Sterile conditions: < 0.1% a.r. after 90d [14C-Phenyl] label (n=1), normal application rate (0.5 mg/kg), 20°C
Non-extractable residues after 100 days ‡	25.1 – 46.3% a.r. after 120/180d [14C-Phenyl] label (n=4), normal application rate (0.5 mg/kg), 20°C 30.6 – 41.3% a.r. after 180d [14C-Dodecyl] label (n=2), normal application rate (0.5 mg/kg), 20°C 55.9% a.r. after 120d [14C-Phenyl] label (n=1), normal application rate (0.5 mg/kg), 10°C Sterile conditions: 7.8% a.r. after 90d [14C-Phenyl] label (n=1), normal application rate (0.5 mg/kg), 20°C
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	R1 (2-dodecyl-3-hydroxy-1,4-naphtalenedione) - 15.7 – 33.8% a.r. after 2 – 10d (n = 4) AKM-18 (2-(1',2'-dioxotetradecyl) benzoic acid) 4.3 – 21.9% a.r. after 2 – 7d (n = 4) [14C-Phenyl] and [14C-Dodecyl] labels

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

Anaerobic degradation ‡

Mineralization after 100 days	2.8% after 365d
Non-extractable residues after 100 days	5.1% a.r. after 365d
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	R1 – 41.1% a.r. after 7d AKM-18 – 23.2% a.r. after 269d [14C-Phenyl] label
Soil photolysis ‡	Mineralisation – 3.0% after 13d Non-extractable residues 12.9% a.r. after 13d
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	Metabolites (Irradiated test) AKM-18 – 23.7% a.r. after 6d Metabolite A – 13.8% a.r. after 2d Polars – 26.2% a.r. after 13d

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

	[^{14}C-Phenyl] label Metabolites (Non-Irradiated test) R1 – 10.4% a.r. after 13d AKM-18 – 46.1% a.r. after 6d Metabolite A – 15.9% a.r. after 13d Polars – 23.4% a.r. after 13d [^{14}C-Phenyl] label

Soil adsorption/desorption (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

K_f / K_{oc}	K_{oc}: parent 39900 – 123000 L/kg (mean 66033 L/kg, 1/n could not be determined, **4** 3 soils) Kf_{oc} R1: 9000 – 230000 L/kg (mean 100666 L/kg, 1/n = 0.6 – 1.0, **4** 3 soils) Kf_{oc} AKM-18: 9697 – 67000 L/kg (mean 43081 L/kg, 1/n = 1.30 – 1.62, 4 soils) indicative values only
K_d	K_d: parent 678 –1620 L/kg (mean 1020 L/kg, **4** 3 soils) R1: 72 – 3400 L/kg (mean 1284 L/kg, **4** 3 soils) AKM-18: 201 – 686 L/kg (mean 355 L/kg, 4 soils) indicative values only
pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	No data, not required

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

Column leaching ‡	Guideline: BBA Guidelines, Part IV, 4-2 Precipitation (mm): 200 mm Time period (d): 2d Leachate: < 1% a.r. total residues/ radioactivity in leachate in three soils, 4% a.r. total residues/ radioactivity in leachate in one soil, which was later identified as polar radioactive material > 74% total residues/ radioactivity retained in top 10 cm.
Aged residues leaching ‡	Guideline: BBA Guidelines, Part IV, 4-2 Precipitation (mm): 200 mm Time period (d): 2d Leachate: < 1% a.r. total residue / radioactivity in leachate > 73% total residues/ radioactivity retained in top 5 cm.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Lysimeter/ field leaching studies ‡	No data submitted and no data required.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent	DT_{50}: 2.7 d (worst case lab studies)
Method of calculation	First-order
Application data	Crop: apples and ornamentals % plant interception: 80% apples and 50% ornamentals Number of applications: 1 for apples and ornamentals in the field; 3 for ornamentals in glasshouses Interval (d): 7 Application rate(s): 281 g as/ha (apples) 600 g as/ha (ornamentals)

Actual TWA PECs (mg/kg) of acequinocyl following application in orchards and ornamentals in the field and in glasshouses.

Day after application	Orchards apples (0.281 kg a.s./ha)		Ornamentals in the field (0.600 kg a.s./ha)		Ornamentals in glasshouses (0.600 kg a.s./ha; 3 times)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	0.075	0.075	0.400	0.400	0.483	0.483
1	0.059	0.066	0.312	0.354	0.377	0.428
2	0.046	0.059	0.244	0.315	0.295	0.381
4	0.028	0.048	0.149	0.254	0.180	0.307
7	0.013	0.036	0.071	0.190	0.085	0.230
14	0.002	0.021	0.013	0.112	0.015	0.135
21	<0.001	0.014	0.002	0.077	0.003	0.092
28	<0.001	0.01	<0.001	0.058	<0.001	0.070
50	<0.001	0.006	<0.001	0.032	<0.001	0.039
100	<0.001	0.003	<0.001	0.016	<0.001	0.020

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Metabolite R1	DT_{50}: 33d (worst case lab studies)
Method of calculation	First-order
Application rate	Crop: apples and ornamentals % plant interception: 80% apples and 50% ornamentals Number of applications: 1 for apples and ornamentals in the field; 3 for ornamentals in glasshouses Interval (d): 7 Application rate(s): 281 g as/ha (apples) 600 g as/ha (ornamentals) (assumed R1 is formed at a maximum of 33.8% of the applied dose)

Actual and TWA PECs (mg/kg) of the major metabolite R1 following application of acequinocyl in orchards (0.281 kg a.s./ha for apples, resulting in a maximum of 85 g R1/ha) and ornamentals (0.600 kg a.s./ha, resulting in a maximum of 181 g R1/ha) in the field and in glasshouses.

Days after application	Orchards apples (0.85 kg R1/ha)		Ornamentals in the field (0.181 kg R1/ha)		Ornamentals in glasshouses (0.181 kg R1/ha; 3 times)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	0.023	0.023	0.121	0.121	0.315	0.315
1	0.022	0.022	0.118	0.119	0.308	0.311
2	0.022	0.022	0.116	0.118	0.302	0.308
4	0.021	0.022	0.111	0.116	0.289	0.302
7	0.020	0.021	0.104	0.112	0.272	0.293
14	0.017	0.020	0.09	0.105	0.235	0.273
21	0.015	0.018	0.078	0.098	0.202	0.255
28	0.013	0.017	0.067	0.091	0.175	0.238
50	0.008	0.014	0.042	0.075	0.110	0.195
100	0.003	0.009	0.015	0.050	0.039	0.132

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Metabolite AKM-18	DT_{50}: 3.5-days (worst case lab studies)
Method of calculation	First-order
Application rate	Crop: apples and ornamentals % plant interception: 80% apples and 50% ornamentals Number of applications: 1 for apples and ornamentals in the field; 3 for ornamentals in glasshouses Interval (d): 7 Application rate(s): 281 g as/ha (apples) 600 g as/ha (ornamentals) (assumed AKM 18 is formed at a maximum of 21.9% of the applied dose)

Actual and TWA PECs (mg/kg) of the major metabolite AKM-18 following application of acequinocyl in orchards (0.281 kg a.s./ha for apples, resulting in a maximum of 56 g AKM-18/ha) and ornamentals (0.600 kg a.s./ha, resulting in a maximum of 118 g AKM-18/ha) in the field and in glasshouses.

Days after application	Orchards apples (0.56 kg AKM-18/ha)		Ornamentals in the field (0.118 kg AKM-18/ha)		Ornamentals in glasshouses (0.118 kg AKM-18/ha)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	0.015	0.015	0.079	0.079	0.103	0.103
1	0.012	0.014	0.065	0.071	0.085	0.094
2	0.010	0.012	0.053	0.065	0.096	0.085
4	0.007	0.010	0.036	0.054	0.047	0.071
7	0.004	0.008	0.020	0.043	0.026	0.056
14	0.001	0.005	0.005	0.027	0.006	0.035
21	<0.001	0.004	0.001	0.019	0.002	0.024
28	<0.001	0.003	<0.001	0.014	<0.001	0.019
50	<0.001	0.002	<0.001	0.008	<0.001	0.01
100	<0.001	0.001	<0.001	0.004	<0.001	0.005

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH4: 25ºC, DT_{50} 74 days R1: 23 % AR (30 d, incubation at 25°C) AKM-18: 11% AR
	pH7: 25ºC, DT_{50} 52 hours R1: 55 % AR (96 h, incubation at 25°C) AKM-18: 16.9% AR

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

	pH9: 25ºC, DT_{50} 67 minutes R1: 49 % AR (90 min, incubation at 25°C) AKM-18: 14.6% AR
Photolytic degradation of active substance and metabolites above 10 % ‡	Xenon lamp >290 nm, pH sterile 5 buffer ; DT50 14 minutes AKM-08: 12.9% AR (120 min after irradiation) o-phthalic acid : 12.7% (24 h, end of study)
Quantum yield of direct phototransformation in water at Σ > 290 nm	Φ = 0.065
Readily biodegradable ‡ (yes/no)	No

Degradation in water / sediment

-DT_{50} water -DT_{90} water -DT_{50} whole system -DT_{90} whole system	Due to the limited amount of data > LOQ (estimated by RMS), no reliable kinetic analysis is possible for degradation of acequinocyl and its metabolites in the water phase. However, estimations could be made with the measured concentrations at successive time intervals: < 0.25 and < 0.75d (n = 2) < 2d (n = 2) 0.42 – 0.47d (1st order, r^2 = 0.94 – 0.98, n = 2) 1.4 – 1.6d (1st order, r^2 = 0.94 – 0.98, n = 2)
Mineralisation	30.2 – 32.6% a.r. (at 100 d, study end, n = 2)
Non-extractable residues	46.4 –56.4% a.r. (at 100 d, study end, n = 2)
Distribution in water / sediment systems (active substance)	Maximum of 8.4 –26.4% a.r. in sediment after 0.25 – 1 days. DT_{50} values in sediment could not be determined
Distribution in water / sediment systems (metabolites)	Water: CBAA (2-(carboxycarbonyl)benzoic acid) max of 9.6 – 11.3% a.r. (2-4 days, n = 2 [DT_{50} could not be determined]) R1: max 12% AR at 0d [DT_{50} could not be determined] Sediment: AKM-18 max of 15.3 –19.0% a.r. (1 day, n= 2 [DT_{50} could not be determined])

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

Parent	DT_{50}: < 0.75d Kinetics: 1st order (from water phase)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Application rate	Crop: apples and ornamentals Number of applications: max 1 for apples and 3 for ornamentals Interval (d): 7 Application rate(s): 281 g as/ha (apples) 600 g as/ha (ornamentals) Depth of water body: 30 cm
Main routes of entry	29.2% drift from 3 meter (apples) 8.02% drift from 3 meter (ornamentals)

Actual and TWA PECsw actual (µg/L) of acequinocyl following early application at maximum dose (281 g a.s./ha) to orchards.

Day after application	Orchards, early application; actual and TWA PECsw of acequinocyl at distance (drift %)					
	3 m (29.2)		5 m (19.89)		10 m (11.81)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	27.35	27.35	18.63	18.63	11.06	11.06
1	10.85	17.85	7.39	12.16	4.39	7.22
2	4.31	12.47	2.93	8.49	1.74	5.04
4	0.68	7.22	0.46	4.92	0.27	2.92
7	0.04	4.22	0.03	2.88	0.02	1.71
14	<0.01	2.11	<0.01	1.44	<0.01	0.86
21	<0.01	1.41	<0.01	0.96	<0.01	0.57
28	<0.01	1.06	<0.01	0.72	<0.01	0.43
50	<0.01	0.59	<0.01	0.40	<0.01	0.24
100	<0.01	0.30	<0.01	0.20	<0.01	0.12

Day after application	Orchards, early application; actual and TWA PECsw of acequinocyl at distance (drift %)					
	15 m (5.55)		30 m (1.04)		50 m (0,3)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	5.20	5.20	0.97	0.97	0.28	0.28
1	2.06	3.39	0.39	0.64	0.11	0.18
2	0.82	2.37	0.15	0.44	0.04	0.13
4	0.13	1.37	0.02	0.26	0.01	0.07
7	0.01	0.80	<0.01	0.15	<0.01	0.04
14	<0.01	0.40	<0.01	0.08	<0.01	0.02
21	<0.01	0.27	<0.01	0.05	<0.01	0.01
28	<0.01	0.20	<0.01	0.04	<0.01	0.01

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Day after application	Orchards, early application; actual and TWA PECsw of acequinocyl at distance (drift %)					
	15 m (5.55)		30 m (1.04)		50 m (0,3)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
50	<0.01	0.11	<0.01	0.02	<0.01	0.01
100	<0.01	0.06	<0.01	0.01	<0.01	<0.01

Actual and TWA PECsw actual (µg/L) of acequinocyl following late application at maximum dose (281 g a.s./ha) to orchards.

Day after application	Orchards, late application; actual and TWA PECsw of acequinocyl at distance (drift %)					
	3 m (15.73)		5 m (8.41)		10 m (3.60)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	14.73	14.73	7.88	7.88	3.37	3.37
1	5.85	9.17	3.13	5.14	1.34	2.20
2	2.32	6.72	1.24	3.59	0.53	1.54
4	0.37	3.89	0.20	2.08	0.08	0.89
7	0.02	2.27	0.01	1.22	0.01	0.52
14	<0.01	0.76	<0.01	0.41	<0.01	0.17
21	<0.01	1.14	<0.01	0.61	<0.01	0.26
28	<0.01	0.57	<0.01	0.30	<0.01	0.13
50	<0.01	0.32	<0.01	0.17	<0.01	0.07
100	<0.01	0.16	<0.01	0.09	<0.01	0.04

Day after application	Orchards, late application; actual and TWA PECsw of acequinocyl at distance (drift %)					
	15 m (1.81)		30 m (0.54)		50 m (0.22)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	1.70	1.70	0.51	0.51	0.21	0.21
1	0.67	1.11	0.20	0.33	0.08	0.13
2	0.27	0.77	0.08	0.23	0.03	0.09
4	0.04	0.45	0.01	0.13	0.01	0.05
7	<0.01	0.26	<0.01	0.08	<0.01	0.03
14	<0.01	0.13	<0.01	0.04	<0.01	0.02
21	<0.01	0.09	<0.01	0.03	<0.01	0.01
28	<0.01	0.07	<0.01	0.02	<0.01	0.01
50	<0.01	0.04	<0.01	0.01	<0.01	<0.01
100	<0.01	0.02	<0.01	0.01	<0.01	<0.01

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Actual and TWA PECsw (µg/L) of acequinocyl following application at maximum dose (600 g a.s./ha) to ornamentals < 50 cm height in the field.

Day after application	Ornamentals < 50 cm; actual and TWA PECsw of acequinocyl at distance (drift %)					
	1 m (2.77)		5 m (0.57)		10 m (0.29)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	5.54	5.54	1.14	1.14	0.58	0.58
1	2.20	3.62	0.45	0.74	0.23	0.38
2	0.87	2.53	0.18	0.52	0.09	0.26
4	0.14	1.46	0.03	0.30	0.01	0.15
7	0.01	0.86	<0.01	0.18	<0.01	0.09
14	<0.01	0.43	<0.01	0.09	<0.01	0.05
21	<0.01	0.20	<0.01	0.06	<0.01	0.02
28	<0.01	0.21	<0.01	0.04	<0.01	0.02
50	<0.01	0.12	<0.01	0.03	<0.01	0.01
100	<0.01	0.06	<0.01	0.01	<0.01	0.01

Day after application	Ornamentals < 50 cm; actual and TWA PECsw of acequinocyl at distance (drift%)					
	15 m (0.2)		30 m (0.10)		50 m (0.06)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	0.40	0.40	0.20	0.20	0.12	0.12
1	0.16	0.26	0.08	0.13	0.05	0.08
2	0.06	0.18	0.03	0.09	0.02	0.06
4	0.01	0.11	0.01	0.05	<0.01	0.03
7	<0.01	0.06	<0.01	0.03	<0.01	0.02
14	<0.01	0.03	<0.01	0.02	<0.01	0.01
21	<0.01	0.02	<0.01	0.01	<0.01	0.01
28	<0.01	0.02	<0.01	0.01	<0.01	0.01
50	<0.01	0.01	<0.01	<0.01	<0.01	<0.01
100	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Actual and TWA PECsw (µg/L) of acequinocyl following application at maximum dose (600 g a.s./ha) to ornamentals > 50 cm height in the field.

Day after application	Ornamentals > 50 cm; actual and TWA PECsw of acequinocyl at distance (drift %)					
	3 m (8.02)		5 m (3.62)		10 m (1.23)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	16.04	16.04	7.24	7.24	2.46	2.46
1	6.37	10.47	2.84	4.73	0.98	1.61
2	2.53	7.31	1.14	3.30	0.39	1.12
4	0.40	4.23	0.18	1.91	0.06	0.65
7	0.03	2.48	0.01	1.12	<0.01	0.38
14	<0.01	1.24	<0.01	0.56	<0.01	0.19
21	<0.01	0.83	<0.01	0.37	<0.01	0.13
28	<0.01	0.62	<0.01	0.28	<0.01	0.10
50	<0.01	0.35	<0.01	0.16	<0.01	0.05
100	<0.01	0.17	<0.01	0.08	<0.01	0.03

Day after application	Ornamentals > 50 cm; actual and TWA PECsw of acequinocyl at distance (drift %)					
	15 m (0.65)		30 m (0.22)		50 m (0.10)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	1.30	1.30	0.44	0.44	0.20	0.20
1	0.52	0.85	0.18	0.29	0.08	0.13
2	0.21	0.59	0.07	0.20	0.03	0.09
4	0.03	0.34	0.01	0.12	0.01	0.05
7	<0.01	0.20	<0.01	0.07	<0.01	0.03
14	<0.01	0.10	<0.01	0.03	<0.01	0.02
21	<0.01	0.07	<0.01	0.02	<0.01	0.01
28	<0.01	0.05	<0.01	0.02	<0.01	0.01
50	<0.01	0.03	<0.01	0.01	<0.01	<0.01
100	<0.01	0.01	<0.01	0.01	<0.01	<0.01

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Actual and TWA PECsw (µg/L) of acequinocyl following application at maximum dose (600 g a.s./ha) to ornamentals in glasshouses, with a maximum of 3 applications at 7 days interval.

Day after Application	Ornamentals; Actual and TWA PECsw of acequinocyl at 0.1% drift following application in glasshouses	
	Actual PEC	TWA PEC
0	0.20	0.20
1	0.08	0.13
2	0.03	0.09
4	0.01	0.05
7	<0.01	0.03
14	<0.01	0.02
21	<0.01	0.01
28	<0.01	0.01
50	<0.01	<0.01
100	<0.01	<0.01

Maximum PECsw (µg/L) of major metabolites following application at maximum dose (281 g a.s./ha for orchards and 600 g a.s./ha for ornamentals).

Application	Distance (drift%)	Max. PECsw (µg/L) major metabolites	
		R1 (max. formation 12%)	CBAA (max formation 11.3%
Orchards	3 m (29.2%)	2.92	1.56
Ornamentals <50 cm	1 m (2.77%)	0.59	0.32
Ornamentals >50 cm	3 m (8.02%)	1.71	0.92
Ornamentals in glasshouses	-	0.02	0.01

PEC (sediment)

Parent Method of calculation	As the RA for both the parent and the metabolite AKM-18 is based on a spiked water sediment dweller test there is no need for PECsed values for a GAP with one application per season

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

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Model(s) used: PEARL Scenarios (list of names): Chateaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

	Crop: apples, and crops selected as substitutes for ornamentals: vines, strawberries, sunflowers Mean parent DT_{50lab} 2.0d (20°C). Kom: parent, mean 38341, 1/n= 0.9 Metabolite R1: Max. 33.8% of applied dose, Mean DT_{50lab} 12.7d (20 °C). Kom: 57700 L/kg Metabolite AKM 18: Max. 21.9% of applied dose Mean DT_{50lab} 3.5 d (20 °C). Kom: 25114 L/kg indicative value
Application rate	Application rate: 281 g as/ha (apples) 600 g as/ha (ornamentals) crop interception: 80% for apples, 50% of ornamentals No. of applications: max. 1 for apples max. 3 for ornamentals Time of application (month or season): 1st of May (apples); 1st of May and 1st of September (ornamentals)

PEC_{GW}

Maximum concentration	Not calculated
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance.)	Annual average concentrations (80th percentile) according to FOCUS guidance: active substance: < 0.001 µg/L R1: <0.001 µg/L AKM 18: <0.001 µg/L (see detailed results in tables below)

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m)

	Scenario	Parent (µg/L)		Metabolite (µg/L)		
		Early application (May)	Late application (September)	1	2	3
Pearl /pome fruit (apples)	Chateaudun	<0.001	<0.001			
	Hamburg	<0.001	<0.001			
	Jokioinen	<0.001	<0.001			
	Kremsmünster	<0.001	<0.001			
	Okehampton	<0.001	<0.001			
	Piacenza	<0.001	<0.001			
	Porto	<0.001	<0.001			
	Sevilla	<0.001	<0.001			
	Thiva	<0.001	<0.001			

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Pearl /ornamentals (vine)	Scenario	Parent (µg/L)		Metabolite (µg/L)		
		Early application (May)	Late application (September)	1	2	3
	Chateaudun	<0.001	<0.001			
	Hamburg	<0.001	<0.001			
	Kremsmünster	<0.001	<0.001			
	Piacenza	<0.001	<0.001			
	Porto	<0.001	<0.001			
	Sevilla	<0.001	<0.001			
	Thiva	<0.001	<0.001			

Pearl /ornamentals (strawberries)	Scenario	Parent (µg/L)		Metabolite (µg/L)		
		Early application (May)	Late application (September)	1	2	3
	Hamburg	<0.001	<0.001			
	Jokioinen	<0.001	<0.001			
	Kremsmünster	<0.001	<0.001			
	Sevilla	<0.001	<0.001			

Pearl /ornamentals (sunflowers)	Scenario	Parent (µg/L)		Metabolite (µg/L)		
		Early application (May)	Late application (September)	1	2	3
	Piacenza	<0.001	<0.001			
	Sevilla	<0.001	<0.001			

$PEC_{(gw)}$ From lysimeter / field studies

Parent / metabolite	1st year	2nd year	3rd year
Not available – not required			

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

Direct photolysis in air ‡	Not studied – no data requested
Quantum yield of direct phototransformation	Not available and not required

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Photochemical oxidative degradation in air ‡	DT_{50} of 1.21h, derived by the Atkinson method of calculation (12 h day)
Volatilisation ‡	Vapour pressure: 1.69 x 10-6 Pa (at 25 °C)) Henry's Law constant: unit less coefficient 3.9 x 10-5 (calculated)
Metabolites	No data available, no data required

PEC (air)

Method of calculation	Not calculated

$PEC_{(a)}$

Maximum concentration	Expected negligible (DT_{50} 1.21h)

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil:	acequinocyl, R1 and AKM-18
	Surface water:	acequinocyl, R1 and CBAA
	Sediment:	acequinocyl, AKM 18
	Ground water:	acequinocyl, R1 and AKM-18
	Air:	acequinocyl

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

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

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

Potential candidate for R53.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.6: Effects on non-target Species

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

Acute toxicity to mammals	LD_{50} > 4855 mg a.s./kg bw
Acute toxicity to birds	Tests with active substance: LD_{50} > 1942 mg a.s./kg bw (Japanese quail) LD_{50} > 1942 mg a.s. /kg bw (Mallard duck) Test with plant protection product: LD_{50} > 300 mg a.s./kg bw (Bobwhite quail)
Dietary toxicity to birds	Tests with active substance: LD_{50} > 847 mg a.s./kg bw (Japanese quail) LD_{50} > 1335 mg a.s./kg bw (Mallard duck) Test with plant protection product: LD_{50} > 159 mg a.s./kg bw (Bobwhite quail)
Reproductive toxicity to birds	NOEL = 217 mg a.s./kg bw (Bobwhite quail) NOEL = 7.48 mg a.s./kg bw (Mallard duck)
Reproductive toxicity to mammals	NOAEL = 6.9 mg a.s./kg bw (rat)

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

Toxicity/exposure ratios for **birds**

Assessment in agreement with Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC (Working Document Sanco/4145/2002).

Acute Toxicity Exposure Ratios for exposure of birds to acequinocyl, due to consumption of contaminated small insects, leaves and drinking water.

Application	dose (kg a.s./ ha)	bird type	approx. body weight (g)	route	DFI (g/ day)	DWI	LD_{50} (mg/kg bw)	PECfeed or PECwater (mg/kg wwt or µg/L)	ETE (mg/kg bw/d)	TERa
orchards	0.281	Insecti-vorous bird	10	small insects	10.4	2.7	> 1942	14.6	15	> 128
				water				27.4	0.0074	> $2.63*10^5$
ornamen-tals (field)	0.600	Insecti-vorous bird	10	small insects	10.4	2.7	> 1942	31.2	32	> 60
				water				16.0	0.0043	> $4.49*10^5$
ornamen-tals (field)	0.600	Medium herbivorous bird	300	leafy crops	228	26.3	> 1942	52.2	40	> 49
				water				16.0	0.0014	> $1.38*10^5$

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Application	dose (kg a.s./ ha)	bird type	approx. body weight (g)	route	DFI (g/ day)	DWI	LD_{50} (mg/kg bw)	PECfeed or PECwater (mg/kg wwt or µg/L)	ETE (mg/kg bw/d)	TERa
ornamentals (glasshouse)	0.600	Insectivorous bird	10	water	-	2.7	> 1942	0.2	0.000054	$> 3.60*10^7$
ornamentals (glasshouse)	0.600	Medium herbivorous bird	300	water	-	26.3	> 1942	0.2	0.00002	$> 1.10*10^8$

Short-term Toxicity Exposure Ratios for exposure of birds to acequinocyl due to consumption of contaminated small insects and leaves.

Application	dose (kg as/ha)	bird type	approx. body weight (g)	route	DFI (g/day)	LC_{50} (mg/kg bw/d)	PEC_{FEED} (mg/kg wwt)	ETE (mg/kg bw/d)	TERst
orchards (late)	0.281	Insectivorous bird	10	small insects	10.4	> 847	8.2	8.5	> 100
ornamentals	0.600	Insectivorous bird	10	small insects	10.4	> 847	17.4	18	> 47
ornamentals	0.600	Medium herbivorous bird	300	leafy crops	228	> 847	24	18	> 47

Long-term Toxicity Exposure Ratios for exposure of birds to acequinocyl, due to consumption of contaminated small insects and leaves.

Application	dose (kg a.s./ha)	bird type	approx. body weight (g)	route	DFI (g/day)	NOEC (mg/kg bw/d)	PEC_{FEED} (mg/kg wwt)	TWA correction	ETE (mg/kg bw/d)	TERlt
orchards	0.281	Insectivorous bird	10	small insects	10.4	7.48	8.2	-	8.5	**0.88**
ornamentals	0.600	Insectivorous bird	10	small insects	10.4	7.48	17.4	-	18	**0.42**
ornamentals	0.600	Medium herbivorous bird	300	leafy crops	228	7.48	24.0	0.53	10	**0.75**

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Refined long-term Toxicity Exposure Ratios for exposure of birds to acequinocyl, due to consumption of contaminated small insects and leaves, based on revised DT_{50}-values for degradation of residues

Application	dose (kg a.s./ha)	bird type	approx. body weight (g)	route	DFI (g/day)	NOEC (mg/kg bw/d)	PEC_{FEED} (mg/kg wwt)	TWA correction	ETE (mg/kg bw/d)	TERlt
orchards	0.281	Insectivorous bird	10	small insects	10.4	7.48	8.2	<0.205	<1.74	>4.3
ornamentals	0.600	Insectivorous bird	10	small insects	10.4	7.48	17.4	<0.205	<3.7	>2.0
ornamentals	0.600	Medium herbivorous bird	300	leafy crops	228	7.48	24.0	0.53	10	**0.75**

Long-term NOEL birds	7.48 mg/kg bw/d
BCF (earthworms)	12 (calculated value: BCF = (0.84+0.01 Kow)/focKoc
BCF (fish)	366 (experimental value)
Absorption, distribution, excretion and metabolism in mammals	Potential for bioaccumulation: none. Highest transitory dose: 3-9 hr (low dose) and 24-48 hr (high dose)
Kow	1584893 (log Pow = 6.2)
Koc	66033 L/kg
PECsoil	0.077 mg/kg (highest time-weighted-average after 3 weeks)
PECsurface water	1.41 µg/L (highest time-weighted-average after 3 weeks)

Food chain from earthworm to earthworm-eating birds, based on a calculated BCF of 12

Application	dose (kg a.s./ha)	PECsoil (mg/kg) (after 3 weeks)	PECworm (mg/kg)	Daily dose birds (mg/kg bw/d)	TER birds
Orchards	0.281	0.014	0.17	0.19	39.4
Ornamentals (field)	0.600	0.077	0.92	1.02	7.3

Food chain from earthworm to earthworm-eating birds, based on a experimental BCF of 1.86

Application	dose (kg a.s./ha)	PECsoil (mg/kg) (after 3 weeks)	PECworm (mg/kg)	Daily dose birds (mg/kg bw/d)	TER birds
Orchards	0.281	0.014	0.026	0.029	258
Ornamentals (field)	0.600	0.077	0.143	0.157	47.6

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Food chain from fish to fish-eating birds

Application	dose (kg a.s./ha)	PECsurface water (µg/L) (twa after 3 weeks)	PECfish (mg/kg)	Daily dose birds (mg/kg bw/d)	TER birds
orchards	0.281	1.41	0.52	0.11	68
Ornamentals (field)	0.600	0.83	0.30	0.064	116
Ornamentals (glasshouse)	0.600	0.01	0.0037	0.00077	9714

Toxicity/exposure ratios for **mammals** (Annex IIIA, points 10.3)

Assessment in agreement with Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC (Working Document Sanco/4145/2002).

Acute Toxicity Exposure Ratios for exposure of mammals to acequinocyl due to consumption of contaminated grass and leafy crops and drinking water.

Application	dose (kg as/ha)	mammal type	approx. body weight (g)	route	DFI (g/day)	DWI	LD_{50} (mg/kg bw/d)	PEC_{feed} or PEC_{water} (mg/kg wwt or µg/L)	ETEfeed or ETEwater (mg/kg bw/d)	TERa feed or TERa water
Orchards	0.281	small herbivorous mammal	25	grasses	34.80		> 4855	23.9	33	146
				water		5.0		27.4	0.0055	$8.9*10^5$
Ornamentals (field)	0.600	medium herbivorous mammal	3000	leafy crops	832.0		> 4855	52.2	14	335
				water		123.2		16.0	0.0007	$7.4*10^6$
Ornamentals (glasshouse)	0.600	medium herbivorous mammal	3000	water		123.2	> 4855	0.2	0.00001	$5.9*10^8$

Short-term risk assessment

Only conducted or birds (in agreement with the guidance in Sanco/4145/2002).

Long-term Toxicity Exposure Ratios (First Tier) for exposure of mammals to acequinocyl due to consumption of contaminated grass and leaves

application	dose (kg a.s./ha)	mammal type	approx. body weight (g)	route	DFI (g/day)	NOAEL (mg/kg bw/d)	PEC_{FEED} (mg/kg wwt)	TWA correc-tion	ETE (mg/kg bw/d)	TERlt
Orchards	0.281	small herbivorous mammal	25	grasses	34.80	6.9	13	0.53	10	**0.69**
Ornamentals (field)	0.600	medium herbivorous mammal	3000	leafy crops	832.0	6.9	24	0.53	4	**1.73**

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Long-term NOAEL	6.9 mg/kg bw/d
BCF (earthworms)	12 (calculated value BCF = (0.84+0.01Kow)/focKoc)
BCF (fish)	366 (experimental value)
Absorption, distribution, excretion and metabolism in mammals	Potential for bioaccumulation: none. Highest transitory dose: 3-9h (low dose) and 24-48h (high dose
Kow	1584893 (log Pow=6.2)
Koc	66033
PECsoil	0.077 mg/kg (highest time-weighted-average after 3 weeks)
PECsurface water	1.41 µg/L (highest time-weighted-average after 3 weeks)

Food chain from earthworm to earthworm-eating mammals, based on a calculated BCF of 12

Application	dose (kg a.s./ha)	PECsoil (mg/kg) (twa after 3 weeks)	PECworm (mg/kg)	Daily dose mammals (mg/kg bw/d)	TER mammals
Orchards	0.281	0.014	0.17	0.24	28.8
Ornamentals (field)	0.600	0.077	0.92	1.29	5.3

Food chain from earthworm to earthworm-eating mammals, based on a experimental BCF of 1.86

Application	dose (kg a.s./ha)	PECsoil (mg/kg) (twa after 3 weeks)	PECworm (mg/kg)	Daily dose mammals (mg/kg bw/d)	TER mammals
Orchards	0.281	0.014	0.026	0.036	192
Ornamentals (field)	0.600	0.077	0.143	0.200	34.5

Food chain from fish to fish-eating mammals

application	dose (kg a.s./ha)	PECsurface water (µg/L) (twa after 3 weeks)	PECfish (mg/kg)	Daily dose mammals (mg/kg bw/d)	TER birds
orchards	0.281	1.41	0.52	0.07	99
Ornamentals (field)	0.600	0.83	0.30	0.04	173
Ornamentals (glasshouse)	0.600	0.01	0.0037	0.00048	14375

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

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

Group	Test substance	Time-scale	Endpoint	Toxicity (µg a.s./L)
Laboratory tests				
Oncorhynchus mykiss	AKD-2023 Technical	96 h	Mortality, LC_{50}	> aqueous solubility
Cyprinodon variegatus	AKD-2023 Technical	96 h	Mortality, LC_{50}	> aqueous solubility
Lepomis macrochirus	AKD-2023 Technical	96 h	Mortality, LC_{50}	> aqueous solubility
Brachydanio rerio	AKD-2023 Technical	96 h	Mortality, LC_{50}	> aqueous solubility
Daphnia magna	AKD-2023 Technical	48 h	Immobilisation, EC_{50}	3.9
Daphnia magna	AKD-2023 Technical	21 d	Reproduction and growth, NOEC	0.98
Mysidopsis bahia	AKD-2023 Technical	96 h	Mortality, EC_{50}	0.93
Pseudokirchneriella subcapitata	AKD-2023 Technical	72h	Biomass and growth rate, EC_{50}	> aqueous solubility
Cyprinus carpio	metabolite R1	96 h	Mortality, LC_{50}	> aqueous solubility
Oncorhynchus mykiss	metabolite CBAA	96 h	Mortality, LC_{50}	> 100000
Oncorhynchus mykiss	Formulated Product[3)]	96 h	Mortality, LC_{50}	65000
Cyprinidon variegatus	Formulated Product[3)]	96 h	Mortality, LC_{50}	95000
Lepomis macrochirus	Formulated Product[3)]	96 h	Mortality, LC_{50}	> 68000
Oryzias latipes	Formulated Product[3)]	96 h	Mortality, LC_{50}	> 95000
Orconectes virilis	Formulated Product[3)]	96 h	Mortality, LC_{50}	> 98000
Brachydanio rerio	Formulated Product[3)]	96 h	Mortality, LC_{50}	> 90000
Daphnia magna	Formulated Product[3)]	48 h	Immobilisation, EC_{50}	2.36
Daphnia magna[1)]	Formulated Product[3)]	23 d	Population growth	20
Chironomus riparius	Formulated Product[3)]	96 h	Mortality, EC_{50}	> 86000
Macromia magnifica	Formulated Product[3)]	96 h	Mortality, EC_{50}	> 100000
Simocephalus vetulus	Formulated Product[3)]	48 h	Immobilisation, EC_{50}	16.6
Pseudokirchneriella subcapitata	Formulated product[3)]	72 h	Biomass and growth rate, EC_{50}	930
Selenastrum capricornutum	Formulated product[3)]	72 h	Biomass and growth rate, EC_{50}	2000
Chironomus riparius[2)]	Formulated Product[3)]	29 d	emergence and development rate	479

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Outdoor microcosm study:

The outdoor microcosm study can be used to evaluate the ecotoxicological risks of a single application of AKD-2023 15% SC to phytoplankton and zooplankton, including *Chaoborus* sp., typical for a lentic freshwater community. Intended initial concentrations were 0 – 0.5 – 3.0 – 9.0 – 27.0 – 81.0 µg a.s./L. Immediately after application the test compound was mixed in the water layer of the microcosms. For the species groups phytoplankton, zooplankton and *Chaoborus* sp. a NOEAEC of 27 µg a.s./L can be derived. The $NOEC_{community}$ for this study is 9 µg a.s./L, and the $NOEC_{population}$ is 3 µg a.s./L.

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

Acute TERs for acequinocyl from spray drift at several distances for orchards and ornamentals.

Crop	Buffer zone (m)	% drift	LC/EC_{50} (µg a.s./L)*			Actual PECsw (µg a.s./L)	TER		
			fish	daphnia	algae		fish	daphnia	algae
orchards (early)	3	29.2	65000	2.36	930	27.35	2377	**0.09**	34
	5	19.89	65000	2.36	930	18.63	3489	**0.13**	50
	10	11.81	65000	2.36	930	11.06	5877	**0.21**	84
	15	5.55	65000	2.36	930	5.20	12500	**0.45**	179
	30	1.04	65000	2.36	930	0.97	67010	**2.43**	959
	50	0.30	65000	2.36	930	0.28	232142	**8.43**	3321
orchards (late)	3	15.73	65000	2.36	930	14.73	4413	**0.16**	63
	5	8.41	65000	2.36	930	7.88	8249	**0.30**	118
	10	3.60	65000	2.36	930	3.37	19288	**0.70**	276
	15	1.81	65000	2.36	930	1.7	38235	**1.39**	547
	30	0.54	65000	2.36	930	0.51	43333	**4.63**	1824
	50	0.22	65000	2.36	930	0.21	309524	**11.23**	4429
Ornamentals < 50 cm height (field)	1	2.77	65000	2.36	930	5.54	11733	**0.42**	168
	5	0.57	65000	2.36	930	1.14	57018	**2.07**	816
	10	0.29	65000	2.36	930	0.58	112069	**4.07**	1603
	15	0.20	65000	2.36	930	0.40	162500	**5.90**	2325
	30	0.10	65000	2.36	930	0.20	325000	**11.80**	4650
	50	0.06	65000	2.36	930	0.12	541667	**19.66**	7750

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Crop	Buffer zone (m)	% drift	LC/EC$_{50}$ (µg a.s./L)*			Actual PECsw (µg a.s./L)	TER		
			fish	daphnia	algae		fish	daphnia	algae
Ornamentals > 50 cm height (field)	3	8.02	65000	2.36	930	16.04	4052	**0.15**	58
	5	3.62	65000	2.36	930	7.24	8978	**0.33**	128
	10	1.23	65000	2.36	930	2.46	26423	**0.96**	378
	15	0.65	65000	2.36	930	1.30	50000	**1.81**	715
	30	0.22	65000	2.36	930	0.44	147727	**5.36**	2114
	50	0.10	65000	2.36	930	0.20	325000	**11.80**	4650
Ornamentals (glasshouse)	-	0.1	65000	2.36	930	0.2	325000	**11.80**	4650

* values are based on the toxicity tests with the formulation

Chronic TERs (*Daphnia*) for acequinocyl from spray drift at several distances for orchards and ornamentals, based on PECtwa-values

crop	Buffer zone (m)	% drift	NOEC (µg a.s./L)	PECtwa (over 21 d) (µg a.s./L)	TER
orchards (early)	3	29.2	0.98	1.41	**0.70**
	5	19.89	0.98	0.96	**1.02**
	10	11.81	0.98	0.57	**1.72**
	15	5.55	0.98	0.27	**3.63**
	30	1.04	0.98	0.05	19.6
	50	0.30	0.98	0.01	98.0
orchards (late)	3	15.73	0.98	1.14	**0.86**
	5	8.41	0.98	0.61	**1.61**
	10	3.60	0.98	0.26	**3.77**
	15	1.81	0.98	0.09	10.9
	30	0.54	0.98	0.03	32.7
	50	0.22	0.98	0.01	98.0

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

crop	Buffer zone (m)	% drift	NOEC (µg a.s./L)	PECtwa (over 21 d) (µg a.s./L)	TER
ornamentals < 50 cm height (field)	1	2.77	0.98	0.20	**4.90**
	5	0.57	0.98	0.06	16.3
	10	0.29	0.98	0.02	49.0
	15	0.20	0.98	0.02	49.0
	30	0.10	0.98	0.01	98.0
	50	0.06	0.98	0.01	98.0
ornamentals > 50 cm height (field)	3	8.02	0.98	0.83	**1.18**
	5	3.62	0.98	0.37	**2.65**
	10	1.23	0.98	0.13	**7.54**
	15	0.65	0.98	0.07	14.0
	30	0.22	0.98	0.02	49.0
	50	0.10	0.98	0.01	98.0
Ornamentals (glasshouse)	-	0.1	0.98	0.01	98.0

Chronic TERs for *Chironomus riparius* for acequinocyl from spray drift at several distances for orchards and ornamentals

Crop	buffer zone (m)	% drift	NOEC (µg a.s./L)	Actual PECsw (µg a.s./L)	TER
orchards (early)	3	29.2	479	27.35	17.5
orchards (late)	3	15.73	479	14.73	32.5
ornamentals < 50 cm height (field)	1	2.77	479	5.54	86
ornamentals > 50 cm height (field)	3	8.02	479	16.04	30
ornamentals (glasshouse)	-	0.1	479	0.20	2395

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

TERs for acequinocyl from spray drift at several distances for orchards and ornamentals, based on the NOEC-value of 3.0 µg a.s./L

crop	Buffer zone (m)	% drift	NOEC-value	Actual PECsw (µg a.s./L)	TER (invertebrates and algae)
orchards (early)	3	29.2	3.0	27.35	**0.11**
	5	19.89	3.0	18.63	**0.16**
	10	11.81	3.0	11.06	**0.27**
	15	5.55	3.0	5.20	**0.58**
	30	1.04	3.0	0.97	**3.09**
	50	0.30	3.0	0.28	10.7
orchards (late)	3	15.73	3.0	14.73	**0.20**
	5	8.41	3.0	7.88	**0.38**
	10	3.60	3.0	3.37	**0.89**
	15	1.81	3.0	1.7	**1.76**
	30	0.54	3.0	0.51	5.88
	50	0.22	3.0	0.21	14.3
Ornamentals < 50 cm height (field)	1	2.77	3.0	5.54	**0.54**
	5	0.57	3.0	1.14	**2.63**
	10	0.29	3.0	0.58	5.17
	15	0.20	3.0	0.40	7.50
	30	0.10	3.0	0.20	15.0
	50	0.06	3.0	0.12	25.0
Ornamentals > 50 cm height (field)	3	8.02	3.0	16.04	**0.19**
	5	3.62	3.0	7.24	**0.41**
	10	1.23	3.0	2.46	**1.22**
	15	0.65	3.0	1.30	**2.31**
	30	0.22	3.0	0.44	6.82
	50	0.10	3.0	0.20	15.0
Ornamentals (glasshouse)	-	0.1	3.0	0.20	15.0

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Bioconcentration

Bioconcentration factor (BCF)	In carp the BCF for total radioactivity was 366 and 288 at exposure levels of 0.17 and 1.7 µg a.s./L respectively in a bioconcentration test with radiolabelled acequinocyl, the fish homogenate did not contain any acequinocyl or R1.
Annex VI Trigger for the bioconcentration factor (BCF)	100
Clearance time (CT_{50})	0.7 days at 0.17 µg a.s./L (for total radioactivity) 1.3 days at 1.7 µg a.s./L (for total radioactivity)
(CT_{90})	not determined
Level of residues (%) in organisms after the 14 day depuration phase	After the first day of the depuration period, mean concentrations radioactivity in fish had decreased to about 20% of the values at the end of the exposure period.

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

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	48h-LD_{50} > 100 µg a.s./bee	48h-LD_{50} > 100 µg a.s./bee
Preparation (AKD-2023 15% SC)	72h-LD_{50} > 48.5 µg a.s./bee	72h-LD_{50} > 53.9 µg a.s./bee
Metabolite 1	/	/
Field or semi-field tests No data submitted, no study required.		

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

Hazard quotients for honey bees using laboratory toxicity studies on technical acequinocyl and the formulation AKD-2023 15% SC.

crop	dose	oral toxicity		contact toxicity		Annex IV
	(g a.s./ha)	LD_{50} (µg a.s./bee)	hazard quotient	LD_{50} (µg a.s./bee)	hazard quotient	trigger
technical acequinocyl						
orchards	281	> 100	< 2.81	>100	< 2.81	50
ornamentals	600	> 100	< 6	>100	< 6	50
formulation AKD-2023 15% SC						
orchards	281	> 48.5	< 5.8	> 53.9	< 5.2	50
ornamentals	600	> 48.5	< 12.4	> 53.9	< 11.1	50

Acequinocyl does not reveal an IGR-related mode of action. Hence, this compound is not expected to pose a risk to honey bee brood. Data on the effects of acequinocyl on bee brood is therefore not required.

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha)
Typhlodromus pyri ‡	Formulated Product 15.6% (300 g a.s./ha)	7d Mortality Reproduction E-value	8.52 (M_{corr}) 10.04 (7.84)[2)] -17
Typhlodromus pyri ‡	Formulated Product 15.6% (624 g a.s./ha)	7d Mortality Reproduction E-value	4.3 (M_{corr}) 8.18 (7.13)[2)] -10
Aphidius rhopalosiphi ‡	Formulated Product 15% (1050 g a.s./ha)	24h Mortality Reproduction E-value	0 (Mcorr) -2.2 -2.0

2) Number of offspring per female.

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	End point	% effect	Trigger value
Amblyseius andersoni	Protony mph	Formulated Product 15.6%	300	7d Mortality Reproduction E-value	2.15 (M_{corr}) 13.1 (12.1)[2)] -5.7	30
Amblyseius andersoni	Protony mph	Formulated Product 15.8%	624	7d Mortality Reproduction E-value	1.05 (M_{corr}) 4.66 (4.53)[2)] -1.9	30
Poecilius cupreus	Adult	Formulated Product 15.8%	1050	7d Mortality Food consumption E-value	-3.41 (M_{corr}) 4.9 (4.8)[3)] -3.41	30
Aleochara bilineata	Life cycle	Formulated Product 15%	1050	Reproduction	2	30
Pardosa spec.	Adult	Formulated Product 15%	1050	14d Mortality Food consumption	0 (M_{corr}) 42 (39)[4)]	

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	End point	% effect	Trigger value
Chrysoperla carnea Steph.	Larvae	Formulated Product 15%	1050	Mortality	3.5 (M_{corr})	30
Phytoseiulus persimilis	Protony mph	Formulated Product 15.6%	300	Mortality Reproduction E-value	52.5 (M_{corr}) 6.3 (5.9)[2)] 81.2	 30
Phytoseiulus persimilis	Protony mph	Formulated Product 15.8%	600	Mortality Reproduction E-value	-6.0 (M_{corr}) 8.22 (11.19)[2)] 22.6	 30
Aged residue tests						
Typhlodromus pyri	Protony mph	Formulated Product 15.6%	1800	Mortality Reproduction	9.2 (0 days ageing) -2.2[5)] (7 days ageing) +5.1[6)] (0 days ageing) 13.6 (7 days ageing)	50
Phytoseiulus persimilis	Protony mph	Formulated Product 15.6%	1800	Mortality Reproduction	25.0 (0 days ageing) 12.0 (7 days ageing) 1.0 (14 days ageing) 39.4 (0 days ageing) 23.7 (7 days ageing) 45.8 (14 days ageing)	50

1) Values between parentheses are for the control treatment.
2) Number of offspring per female.
3) Number of fly pupae per individual.
4) Number of flies per individual.
5) '-' means less mortality than in the control
6) '+' means a stimulating effect

Field or semi-field tests
No data, not required.

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

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

Acute toxicity	14d-LC_{50} > 1000 mg a.s./kg dw; corrected to 5% o.m. the 14-d LC_{50} > 500 mg a.s./kg dw
Reproductive toxicity	No data, justification given

Toxicity/exposure ratios for soil organisms

Acute risk of acequinocyl to earthworms

Scenario	LC_{50} (mg a.s./kg)	PECs (mg a.s./kg)	Acute TER	Annex VI trigger
Orchards	> 1000	0.075	> 6667	10
Ornamentals (field)	> 1000	0.400	> 1250	10
Ornamentals (glasshouses)	> 1000	0.483	> 1035	10

Effects on other soil macro-organisms

Collembola	According to the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002 rev 2 final, 17 October 2002), laboratory tests on Collembola reproduction are required for persistent substances (DT_{90} >100 days). Acequinocyl is non persistent (DT_{90} values derived from field test 0.3-1.8 days, see Section 2.5.2). A study on the reproduction toxicity of acequinocyl to Collembola is therefore not required.

Effects on soil micro-organisms

Nitrogen mineralization	Effects on nitrification < 25% after 28 and 50 days of exposure in loamy sand soil and sandy loam soil respectively at 7.0 mg a.s/kg soil (5250 g as/ha).
Carbon mineralization	Effects on respiration < 25% after 28 and 29 days of exposure in loamy sand soil and sandy loam soil respectively at 7.0 mg a.s/kg soil (5250 g as/ha).

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

…….	No adverse effects of AKD-2023 15% SC on vegetative vigour with respect to phytotoxicity, biomass, seedling emergence and seedling growth were observed in treated non-target plants at doses of approximately 5.0 kg/ha and 15.0 kg/ha.

‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

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

Test type/organism	Endpoint
Activated sludge	3h-EC_{50} > 974 mg a.s./L
Pseudomonas sp	/

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	Acequinocyl
water	Acequinocyl
sediment	Acequinocyl
groundwater	Acequinocyl

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

Active substance

RMS/peer review proposal	
N;	Harmful
R50/53	Very toxic to aquatic organisms, may cause long term adverse effects t the environment

Preparation

RMS/peer review proposal	
N;	Harmful
R50/53	Very toxic to aquatic organisms, may cause long term adverse effects t the environment

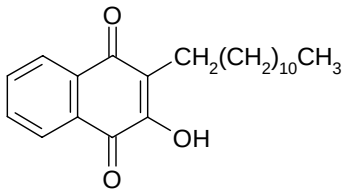
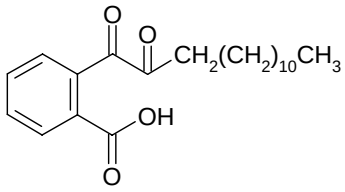
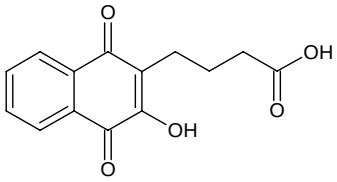
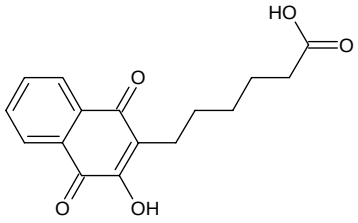
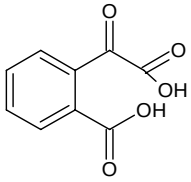
‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

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

LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
R1	2-dodecyl-3-hydroxynaphthalene-1,4-dione	
AKM-18	2-(2-oxotetradecanoyl)benzoic acid	
AKM-14	4-(3-hydroxy-1,4-dioxo-1,4-dihydronaphthalen-2-yl)butanoic acid	
AKM-15	6-(3-hydroxy-1,4-dioxo-1,4-dihydronaphthalen-2-yl)hexanoic acid	
CBAA	2-(carboxycarbonyl)benzoic acid	
AKM-08	2-hydroxy-3-(2-oxoheptyl)naphthalene-1,4-dione