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

mepiquat.

Finalised: 14 April 2008

SUMMARY

Mepiquat is one of the 79 substances of the third stage Part A of the review programme covered by Commission Regulation (EC) No 1490/2002[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within six months a conclusion on the risk assessment to the EU-Commission.

The United Kingdom being the designated rapporteur Member State submitted the DAR on mepiquat in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 5 April 2005. The peer review was initiated on 20 January 2006 by dispatching the DAR for consultation of the Member States and the sole applicant BASF. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and remaining issues were agreed on during a written procedure in January – February 2007. The identified issues as well as further data made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in July and October 2007.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in March 2008 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 plant growth regulator in cereals for stem stabilisation as proposed by the notifier. Full details of the GAP can be found in the attached end points.

The representative formulated product for the evaluation was "Terpal" (BAS 098 00 W), a soluble concentrate (SL) containing 305 g/l mepiquat chloride and 155g/l ethephon.

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

[1] OJ No L 224, 21.08.2002, p. 25, as last amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)

are possible. Adequate methods are available to monitor all compounds given in the respective residue definitions for monitoring for food/feed of plant and animal origin and for environmental matrices, however some validation data are required for the residue method for milk, egg, fat and muscle.

In mammalian toxicity tests, mepiquat-chloride is harmful to rats after oral exposure and is proposed for classification with R22 "Harmful if swallowed" (LD50 464 mg/kg bw, equivalent to 270 mg/kg bw mepiquat). The dermal LD50 of mepiquat-chloride in rats is >2000 mg/kg bw; mepiquat-chloride is proposed for classification as R20, Harmful by inhalation as the LC50 in the rat for mepiquat-chloride was approximately 4.89 mg/l (equivalent to 2.84 mg/L mepiquat), the maximum attainable concentration under the experimental conditions. Mepiquat-chloride is not a skin or eye irritant, nor a sensitiser. The relevant short term toxicity NOAEL is an overall NOAEL of 30.5 mg/kg bw/day from 3- and 12-month study in dog that showed salivation and some mortalities, vacuolisation of the kidney and increased accumulation of siderin in the liver and spleen, whose mechanism and toxicological significance is unclear. Mepiquat-chloride does not show any genotoxic or clastogenic potential in a range of *in vitro* and *in vivo* studies. Mepiquat-chloride does not show any carcinogenic potential either in rats or mice. The relevant NOAEL in long term toxicity studies in rat is 200 mg/kg bw/day. Mepiquat-chloride does not show any reproductive or developmental toxicity potential: the relevant NOAEL for maternal, reproductive and offspring toxicity is 320 mg/kg bw/day based on reduction in viability and lactation indices, body weight and the impaired morphological development in the offspring; in the developmental toxicity study in rats the NOAEL for maternal toxicity is 150 mg/kg bw/day based on clinical signs of toxicity and impaired body weight gain at 300 mg/kg bw/day and for foetotoxicity and teratogenicity 300 mg/kg bw/day based on the absence of any other signs of toxicity at the highest test dose in the study. In a developmental neurotoxicity study, administration of mepiquat resulted in acute lethality for gavaged pups. The ADI is 0.2 mg/kg bw/day based on the NOAEL of 19.9 mg/kg bw/day from the 12-month dietary study in dogs; the AOEL is 0.3 mg/kg bw/day based on the NOAEL of 30.5 mg/kg bw/day from the 90-day study in dogs; the ARfD of 0.3 mg/kg bw for mepiquat-chloride is based on the NOAEL of 30 mg/kg bw/day obtained in the developmental neurotoxicity study. The applied SF is 100. Estimated operator exposure with the German model indicate for operators not wearing PPE levels below the AOEL (10 %) as well as for the UK POEM (70% of the AOEL). Predicted bystander exposure is <1% of the short term systemic AOEL. Workers would not be expected to re-enter treated crops after spraying to perform crop inspection tasks until spray deposits are dry. Estimates of exposure to mepiquat-chloride using data for re-entry exposure contained in the EUROPOEM database indicate exposure levels below the AOEL (3.5%).

The metabolism of mepiquat chloride was investigated in wheat, barley, cotton and grapes. The major component in the crops at harvest was unmetabolised mepiquat. Though rotational crops data were not triggered by the residue behaviour of mepiquat chloride in soil, a metabolism study in rotational crops with radio-labelled substance was submitted. The data indicate that in practice residues above

the limit of quantification of the analytical method are not expected to occur in succeeding and rotational crops.

Currently, only the use of mepiquat chloride on barley would be supported by a sufficient number of valid residue trial data while the notified representative use is on cereals in general. Therefore a data gap for further residue trials was identified.

Animal metabolism studies with ruminants and poultry are available to establish the nature of residues in food of animal origin. Since insufficient data is available to assess the magnitude of residues in cereal grain and straw, the livestock exposure assessment cannot be finalised. Moreover, the residue analysed in the livestock feeding studies does not correspond to the proposed animal residue definition for risk assessment, and further data and information is needed to establish reliable transfer factors of residues in food of animal origin and conversion factors for monitoring.

Therefore the meeting of experts concluded that the consumer risk assessment and MRL proposals cannot be finalised. If deviating from the notified use on cereals a use of mepiquat-chloride on barley only is considered, consumer exposure is expected to be well below the toxicological reference values for mepiquat-chloride and MRLs could be proposed.

With regard to the environmental fate and behaviour data no significant metabolites (>10% AR) were identified in any soil at any time point in laboratory aerobic route and rate of degradation studies using [2,6-^{14}C] mepiquat-chloride. First order DT_{50} values were in the range 6 to 40 d. In laboratory anaerobic metabolism studies and soil photodegradation studies mepiquat-chloride was observed to undergo insignificant degradation, and no DT_{50} values could be calculated. Based on evidence from laboratory soil batch adsorption studies mepiquat chloride can be classified as slight to high mobile in soil ($K_f$oc = 67-4833 mL/g, with a median value of 890 mL/g). For groundwater, the 80th percentile annual average concentrations in leachate leaving the top 1 m soil layer were predicted to be <0.001 µg/L for mepiquat-chloride for all FOCUS scenarios pertinent to use on winter cereals.

In aerobic natural water/sediment systems, mepiquat-chloride dissipated from the water phase by partitioning to sediment with a first order DT_{50} of 6 to 9 d. Peak partitioning of mepiquat-chloride to the sediment was measured 14 to 30 d after dosing at a maximum of 56.2% AR. Mineralisation was significant and by the termination of the study $^{14}CO_2$ represented 61.7-65.8% AR. No significant quantities of metabolites were detected. First order DT_{50} values for the whole system were 32 to 33 d.

Mepiquat-chloride is essentially non-volatile and there is little potential for volatilisation from either soil or plant surfaces. Consequently, air is not a likely route of environmental contamination.

Birds and mammals may be exposed to mepiquat-chloride by intake of insects present in the treated crop. Since mepiquat-chloride is to be applied after BBCH growth stage 31 the crop itself is assumed to be past the stage were it is attractive as food. The acute and short-term TER values for birds are well above the Annex VI triggers in the first tier assessment, hence indicating a low risk. For mammals, both the acute and long-term TER values are well above the triggers, hence the risk to mammals is considered as low. The first-tier long-term TER value for birds is 4.4 and thus below the Annex VI trigger of 5. A new long-term (reproduction) study with birds was presented in an addendum (June 2007) together with a new risk assessment for insectivorous birds based on

yellowhammer (*Emberiza citronella*) as a focal species. The refinement of PT and PD were accepted by the experts and the refined long-term TER of 8.53 was above the trigger of 5.

The risk to birds from the second active substance (ethephon) in the representative formulation "Terpal" was considered in the acute risk assessment presented in the addendum. The acute TERs were still above the trigger and the acute risk from the formulation was considered as sufficiently addressed. A risk assessment for the uptake of contaminated drinking water according to SANCO/4145/2000 was included in the addendum. The acute TERs of >7.3 (birds) and 2.2 (mammals) were below the trigger of 10. No agreement was reached in the expert meeting on the relevance of this exposure route for the suggested use in cereals. It was proposed by the experts that this point should be left open to be considered at MS level after Annex I inclusion since the relevance of this exposure scenario may depend on the local weather conditions and the landscape structure (availability of alternative drinking water sources).

The most sensitive aquatic organism tested and driving the aquatic risk assessment was *Lemna gibba.* The TERs were above the trigger of 10 with FOCUS step 1 PEC_{sw} indicating a low risk. Mepiquat-chloride partitions into sediment, and was found in amounts of 48-56% of applied in the water/sediment studies. However, since the NOEC for *Daphnia* is 12.5 mg/L, which is >0.1 mg/L, a study with sediment dwelling organisms is not required according to SANCO/3268/2001. The log P_{ow} for mepiquat-chloride is <3 and therefore the potential for bioconcentration is considered as low. No major metabolites (≥10%) were detected in the water/sediment study

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

Key words: mepiquat, mepiquat-chloride, peer review, risk assessment, pesticide, plant growth regulator

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000, as amended by Commission Regulation (EC) No 1095/2007 regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Mepiquat is one of the 79 substances of the third stage, part A, covered by the Regulation (EC) No 1490/2002 designating the United Kingdom as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, the United Kingdom submitted the report of its initial evaluation of the dossier on mepiquat, hereafter referred to as the draft assessment report, to the EFSA on 5 April 2005. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1490/2002 on 20 January 2006 to the Member States and the main applicant BASF as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, EFSA and Member States identified and agreed during a written procedure in January – February 2007 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the notifier, a scientific discussion took place in experts' meetings in July and October 2007. 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 during a written procedure with the Member States in March 2008 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).

In accordance with Article 11c (1) of the amended Regulation (EC) No 1490/2002, 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 provided for by the same Article. 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 19 February 2007)

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 19 March 2008).

Given the importance of the draft assessment report including its addendum (compiled version of January 2008 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Mepiquat is the ISO common name for 1,1-dimethylpiperidinium (IUPAC). However the data submitted in the dossier refer to the variant mepiquat chloride (1,1-dimethylpiperidinium chloride).

Mepiquat is a quaternary ammonium plant growth regulator. Mepiquat acts as an inhibitor of the biosynthesis of gibberellic acid. It is absorbed and translocated throughout the plant. Mepiquat is used on cereals to reduce unwanted longitudinal shoot growth without lowering plant productivity.

The representative formulated product for the evaluation was “Terpal”, a soluble concentrate (SL) containing 305 g/l mepiquat-chloride and 155g/l ethephon, registered in several EU member states.

The representative uses evaluated comprise foliar spraying with conventional spraying devices for stem stabilisation on barley, oats, wheat and rye, up to growth stage of BBCH 31-49, in northern EU countries, at a single application at a maximum application rate of 762.5 g a.s./ha (mepiquat chloride).

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

Mepiquat chloride is a variant of mepiquat, however as the data submitted in the dossier refer to the variant, the specification is expressed on the basis of mepiquat chloride. Mepiquat chloride is very hygroscopic and therefore the dry technical material (TC) is not isolated during production, but is diluted with water to give an aqueous technical concentrate (TK). The experts of PRAPeR 31 meeting agreed that the specification should be for the TK. The minimum mepiquat chloride content of the TK is 615 g/l, the maximum content is 665 g/l. (min 990 g/kg of theoretical dry technical concentrate). No FAO specifications exist.

PRAPeR 31 meeting required justification why unidentified impurities are required in the technical specification and to supply technical specification which includes impurities specified in TK and TC (i.e., on dry weight basis). The notifier submitted a corrected specification presented in an addendum to vol.4 (January 2008). The unidentified impurities were removed from the specification and thus the specification for the technical concentrate, with the current specified limit for impurity 1, can be considered as agreed by the meeting of experts.

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 mepiquat chloride or the respective formulation.
The main data regarding the identity of mepiquat chloride and its physical and chemical properties are given in appendix 1.

A CIPAC method (440/TK/M/3) is available for the determination of mepiquat chloride in the technical material and adequate analytical methods based on the CIPAC method are available for the determination of the active substances mepiquat chloride and ethephon in the representative formulation. Adequat method is available as well for the determination of the respective impurities in the technical material (HPLC-UV).

Sufficient test methods and data relating to physical, chemical and technical properties and analytical methods are available to ensure that quality control measurements of the plant protection product are possible.

The residue definition for enforcement was set as the sum of mepiquat and its salts expressed as mepiquat chloride for all commodities.

The applicability of the multi-residue methods to determining residues of mepiquat chloride was assessed, but was found to be unacceptable.
Adequate methods are available to monitor all compounds given in the respective residue definitions in food/feed of plant origin. HPLC-MS/MS methods are available to monitor residues with LOQ 0.05 mg/kg in wheat forage, barley grain, maize straw, grape, apple, oilseed rape seed, wheat grain and various processing products of wheat and barley.
The methods proposed initially for enforcement of residues in animal tissues use hazardous reagents and were considered not acceptable, the alternative HPLC-MS/MS method was validated in liver and kidney with LOQ 0.05 mg/kg. As a consequence a data gap was identified at PRAPeR 31:
-validation data required for the HPLC-MS/MS method in line with SANCO 825/00 for milk, egg, fat and muscle.
Adequate methods are available (ion chromatography with suppressed conductivity detection) to monitor residues according to residue definition in soil, with LOQ of 0.01 mg/kg, in water (drinking

water, surface water) with LOQ of 0.05 µg/kg and in air with LOQ of 0.016 mg/m^3. HPLC-MS/MS methods are available for confirmation for all environmental matrices.

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

2. Mammalian toxicology

Mepiquat was discussed in a meeting of experts in July 2007 (PRAPeR 29).

According to the phys-chem section, the active substance is mepiquat, and mepiquat chloride represents a variant.

In the DAR RMS is referring to either mepiquat or mepiquat-chloride. During the meeting it was noted that there are other mepiquat salts on the market, so mepiquat should be considered the reference substance. However, it was reported that it was not known if or to what extent the effects observed in the different investigations are attributable to mepiquat or to the chloride moiety of the molecule.

From the literature, limited data show that different salts of mepiquat (e.g. pentaborate) might have different metabolic properties possibly influencing the toxicokinetics of the substance. Due to this, the meeting agreed that the molecule under discussion in the mammalian toxicity meeting was mepiquat-chloride and not mepiquat. Values referring to mepiquat-chloride may be expressed as mepiquat ion by multiplying by a factor of 0.77. The meeting also agreed that any other salt of mepiquat has to be shown to be equivalent to mepiquat-chloride in order to apply the present assessment.

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

Mepiquat-chloride is rapidly and extensively absorbed after an oral dose and distributed into organs and tissues. The bioavailability after an oral dose of ≤ 12 mg/kg bw was approximately 85 % of the administered dose. Mepiquat is mainly excreted through the urine. Faecal elimination was of limited relevance, accounting for less than 15 % and was confirmed by studies in bile-cannulated rats to be mainly the result of the unabsorbed substance but this was noted to increase with dietary intake. Mepiquat-chloride apparently is not metabolised in rats before elimination as unchanged in urine.

2.2. Acute toxicity

Mepiquat-chloride is harmful to rats after oral exposure and is proposed for classification with R22 “Harmful if swallowed” (LD50 464 mg/kg bw, equivalent 270 mg/kg bw mepiquat). The dermal LD50 of mepiquat-chloride in rats is >2000 mg/kg bw; the inhalation LC50 in the rat for mepiquat-chloride was approximately 4.89 mg/l (equivalent to 2.84 mg/L mepiquat), the maximum attainable concentration under the experimental conditions, thus mepiquat-chloride is proposed for classification with R20, “Harmful by inhalation”. Mepiquat-chloride is not a skin or eye irritant, nor sensitizing.

2.3. SHORT TERM TOXICITY

Short-term toxicity was investigated in rats, mice and dogs.

Rodents seem to be minimally affected (impaired growth in rats, no effects in mice up to 1000 mg a.s./kg bw/day). Dogs appear to be the most sensitive species: clinical signs included mainly salivation and some mortalities; furthermore dogs showed vacuolisation of the kidney and increased accumulation of siderin in the liver and spleen, whose mechanism and toxicological significance is unclear. The relevant short term toxicity NOAEL is an overall NOAEL of 30.5 mg/kg bw/day from 3- and 12-month study in dog (30.5 and 19.9 mg/kg bw/day, respectively). The NOAEL in a 28-day dermal toxicity study was 1000 mg/kg bw/day (limit dose) based on the absence of any treatment-related findings.

2.4. GENOTOXICITY

Mepiquat-chloride does not show any genotoxic or clastogenic potential in a range of *in vitro* and *in vivo* studies.

2.5. LONG TERM TOXICITY

Chronic toxicity and carcinogenicity studies were conducted in rats and mice.

Rats showed decreased food consumption, body weight and body weight gain, with relevant NOAEL of 200 mg/kg bw/day. Mepiquat-chloride was found to be of relatively low toxicity in mice, with a relevant NOAEL in mice of 296 mg/kg bw/day.

Mepiquat-chloride does not show any carcinogenic potential either in rats or mice.

2.6. REPRODUCTIVE TOXICITY

The reproductive toxicity of mepiquat-chloride was evaluated in two multi-generation studies and developmental toxicity studies in rats and rabbit. The relevant NOAEL for maternal, reproductive and offspring toxicity is 320 mg/kg bw/day based on reduction in viability and lactation indices, body weight and the impaired morphological development in the offspring.

In the developmental toxicity study in rats the NOAEL for maternal toxicity is 150 mg/kg bw/day based on clinical signs of toxicity and impaired body weight gain at 300 mg/kg bw/day and for foetotoxicity and teratogenicity the NOAEL is 300 mg/kg bw/day based on the absence of any other signs of toxicity at the highest test dose in the study.

In summary, mepiquat-chloride does not have any reproductive or developmental toxicity potential.

2.7. NEUROTOXICITY

Studies for delayed neurotoxicity were not performed as the structure of mepiquat-chloride does not suggest a delayed neurotoxicity potential.

In an acute oral neurotoxicity study in rats the NOAEL was 100 mg/kg bw (58 mg a.s./kg bw mepiquat) based on observations of decreased motor activity at 300 mg a.s./kg bw. The clinical effects observed were explained by reactivity with nicotinic and muscarinic receptors and represent a reversible binding to receptors rather than irreversible neurotoxicity.

In a subchronic neurotoxicity study, there was no evidence of neurotoxicity at the highest test dose of 13000 ppm (517 mg/kg bw/day in males and 617 mg/kg bw/day in females). However, the overall NOAEL in the 3-month dietary study with neuropathological assessments was 1625 ppm (66 mg/kg bw/day in males and 79 mg/kg bw/day in females) based on impaired body weight gain at 6500 ppm (259 mg/kg bw/day in males and 367 mg/kg bw/day in females).

In the Addendum to B6 (June 07), the Rapporteur summarised a developmental neurotoxicity (DNT) study conducted by the applicant in response to a requirement made by US EPA.
The RMS concluded that mepiquat-chloride did not exhibit developmental neurotoxicity at dose levels of ≤ 60 mg/kg bw/day, but acute lethality resulted in pups when gavaged between days 11 and 22. The Rapporteur noted that the mortality findings in this study do not correlate with any risk scenario and hence the findings of this study do not impact on the regulatory endpoints and risk assessments provided. During the meeting, it was noted that there was a huge difference between neonatal mortality and adult mortality in the DNT study. The data could be used for the setting of an ARfD since the effects occurred early in the study. The NOAEL of the pups was 30 mg/kg bw/day. RMS pointed that in regard to the effects in pups the developmental studies did not show any neurotoxic effects in the surviving pups. There was also no evidence from the multigeneration studies in support of a neurotoxic effect in pups at that dose level. Two MSs noted that pups died after dosing at day 11, a time point where they cannot be considered as neonates anymore.
The majority of the experts agreed to base the ARfD on the NOAEL of 30 mg/kg bw/day obtained in this developmental neurotoxicity study applying an SF of 100 which would result in an ARfD of 0.3 mg/kg bw/day. The RMS was also asked to clarify whether the NOAEL was referring to mepiquat-chloride or mepiquat only.
EFSA note: after the meeting of experts, the Rapporteur has confirmed with the Notifier and laboratory that the NOAEL of 30 mg/kg bw/day in the DNT study was already corrected for the amount of active substance mepiquat-chloride.

2.8. FURTHER STUDIES

Receptor binding studies have shown that mepiquat-chloride has a preferential affinity for the nicotinic subtype receptor. The agonist activity of the compound is 100 times lower than that of acetylcholine. The affinity to the muscarinic subtype receptor is approximately 5 orders of magnitude lower than that of atropine. Based on these findings it was concluded that the signs of clinical toxicity, as observed at high dose levels in animal studies, are mainly associated with the activation of the nicotinic receptor (tremors, ataxia, lack of motor coordination, decreased motor activity and abnormal posture), whereas some other clinical observations (bradypnea and salivation) may be associated with the activation of the muscarinic receptor. Thus the effects are reversible interactions of mepiquat-chloride with receptors and do not indicate a potential to damage the neurons.

During the meeting of experts the toxicological profile of the 4-hydroxy mepiquat chloride was discussed. Taking into account that the metabolite was tested for acute oral toxicity and *in vitro* genotoxicity (which partially fulfils the requirements of the Guidance Document on the relevance of

groundwater metabolites) it was concluded that the metabolite is of comparable toxicity as the parent compound.

2.9. MEDICAL DATA

The applicant reported that the manufacturing plant personnel are surveyed by regular medical examinations comprising general medical and occupational history, work-related complaints, physical examination, red and white blood cell counts, ALT, AST, GGT, cholinesterase, creatinine, uric acid, cholesterol, triglycerides and urine analysis. No health effects referable to mepiquat-chloride were recorded, as well as cases of incidental exposure.

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

Acceptable Daily Intake (ADI)

The ADI of mepiquat-chloride is 0.2 mg/kg bw/day based on the NOAEL of 19.9 mg/kg bw/day from the 12-month dietary study in dogs, applying a safety factor of 100.

Acute Reference Dose (ARfD)

The ARfD for mepiquat-chloride is based on the NOAEL of 30 mg/kg bw/day obtained in the developmental neurotoxicity study applying an SF of 100 which would result in an ARfD of 0.3 mg/kg bw.

EFSA notes that during the meeting of experts it was highlighted how this approach is very conservative.

Acceptable Operator Exposure Level (AOEL)

The overall AOEL for mepiquat-chloride is 0.3 mg/kg bw/day based on the NOAEL of 30.5 mg a.s./kg bw/day from the 90-day study in dogs. The applied SF is 100.

2.11. DERMAL ABSORPTION

During the meeting of experts, dermal absorption of mepiquat-chloride formulated as Terpal was discussed. The RMS reported that it was not the complete combined formulation that was tested (Terpal is a liquid formulation containing mepiquat-chloride and ethephon). However, it was considered that this should not influence the overall assessment since ethephon (in the batch tested) would not have an impact on the dermal absorption. In addition a very conservative approach has been taken in the evaluation of the data. The meeting agreed to the value of 3% for concentrate and dilution.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

Terpal is proposed to be used on cereals at the maximum dose of 0.7625 kg a.s./ha.

Operator exposure

	Application method (crop)	Systemic exposure (mg/kg bw/day)	% of systemic AOEL
German model	Tractor, field crops	0.029	10
UK POEM	Tractor, hydraulic boom and nozzles	0.209	70

Estimates of exposure to mepiquat-chloride for application of 'BAS 098 00W' via field crop (boom) sprayers derived from German model data, indicate levels of exposure for operators not wearing PPE within the AOEL (10 % of the AOEL), as well as using UK POEM (70% of the AOEL).

Worker exposure

Estimates of exposure to mepiquat-chloride using data for re-entry exposure contained in the EUROPOEM database indicate it is unlikely that the exposure for workers re-entering treated cereal crops will exceed the systemic AOEL. Estimated exposure for re-entry workers is 3.5% of the AOEL.

Bystander exposure

Estimated bystander exposure is <1% of the AOEL.

EFSA notes that the operator, worker and bystander risk assessment should be regarded as inconclusive because Terpal is a combi product, and the influence of ethephon on the risk has not been investigated.

3. Residues

Mepiquat was discussed in the meeting of experts in residues (PRAPeR 30) in July 2007.

It is noted that the chloride salt, a variant of mepiquat, was used in the residue studies. Thus the evaluated data belong to the variant mepiquat chloride and the reported residue levels are expressed as mepiquat chloride, unless otherwise explicitly specified.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of mepiquat was investigated in wheat, barley, cotton and grapes. Formulated ring labelled ^{14}C- mepiquat chloride was applied as a foliar application to the crops. In cereals the rate was approximately equivalent to the notified rate for wheat (0.9N rate) and barley (1.2N rate). No GAP can be specified for cotton and grapes and can be compared with the available data since these uses were not notified as representative uses.

At harvest of the mature cereal crops (52 to 71 days after application) the total ^{14}C residues (TRR; expressed as mepiquat chloride equivalents) were 0.78 mg/kg in wheat grain, 10 mg/kg in wheat straw, 1.8 mg/kg barley grain, and 5.1 mg/kg barley straw.

On extraction and characterisation of the residues one major component was identified as mepiquat that accounted for 72% to 82% of the TRR in grain and straw at harvest. Several unknown polar metabolites were isolated but not further identified as individually they did not represent more than 5% of the TRR. The remaining unextractable radioactivity accounted for about 3-5% TRR (0.05 mg/kg) in barley and wheat grain, 10% TRR in wheat straw (1 mg/kg) and 18% in barley straw (0.9 mg/kg).

A similar picture as in cereals was found in cotton and grapes. The predominant residue at harvest of cotton seed and straw and of grapes 67 and 98 days after application respectively was mepiquat, accounting for greater 90% TRR in cotton and about 77% TRR in the grapes. Several unknown metabolites were isolated but not identified. The non-extractable radioactivity was low (6% TRR or less).

Based on the plant metabolism data submitted for wheat, barley, cotton and grapes it was concluded that the vast majority of residues at harvest is still present as unmetabolised mepiquat. Metabolites were only present at low levels and not further identified. It was postulated that the unextractable radioactivity in the crops at harvest was probably associated with the fragmentation of the ring and the natural incorporation of these fragments into the plant tissue.

It was concluded by the experts in the meeting PRAPeR 30 that the residue definition for both enforcement and risk assessment in plant products should be the sum of mepiquat and its salts, expressed as mepiquat chloride.

There is a total of 9 residue trials available in barley that support a latest application at growth stage (GS) 49; four in accordance with modern standards (2005) and five older trials (1981) of poor quality. However the results of all these trials are consistent, indicating that the older trials in barley could be acceptable though data supporting their validity is lacking. For cereals other than barley no trials are available that support the notified GAP up to GS 49. According to the present guidance it might be acceptable to extrapolate the barley data to the whole group of cereals when application is made up to GS 49 (first awns visible), though experts' views differ on what GS of cereals should be considered as the start of formation of the consumable crop part. However, for plant growth regulators it was acknowledged by the experts that the residue behaviour is very variable as it may differ from one cereal crop to another but also between species or even varieties of the same crop, considering that these compounds by nature interfere with plant metabolism and growth. The experts concluded that it is therefore not acceptable to extrapolate between cereal crops for plant growth regulators.

Considering that the majority of the available residue trials in wheat, barley, oats and rye are from the 1970's or early 1980's and are not in accordance with modern standards, that most of them were performed at an earlier growth stage than GS 49, and that there is a large variability in the results, the experts concluded that 8 additional residue trials are required for wheat with application at GS 49.

It was also concluded that, if significant differences are noted between the wheat and the barley trials, further data may be required for the individual cereals. This requirement appears mainly to be

important for MRL setting, however to finalise the risk assessment (consumer and livestock exposure) a sound residue data base is needed, too, in particular when a great variety of experimental results has been found.

Processing studies carried out on barley and wheat showed that residues of mepiquat in the processed samples had not increased significantly with the exception of wheat bran which had increased by a factor of 3 (the mean factor for all bran fractions). In the case of the other consumable products wholemeal flour, flour and wholemeal bread, residues decreased by a factor of 0.9, 0.2 and 0.6 respectively. Studies on the nature of the residue indicate that mepiquat did not degrade abiotically under conditions representative of industrial or domestic food processing.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Mepiquat has a DT_{90} of less than 100 days and therefore the submission of rotational crop data was not a requirement.

Nevertheless the metabolism and distribution in rotational crops was investigated in lettuce, wheat and radish. The crops were grown in soil that had been treated with ring labelled ^{14}C -mepiquat chloride, at 0.9 N rate compared to cGAP rate. The plant-back intervals were 29 days, 120 days and 365 days, respectively.

The enrichment of radioactivity in the plants indicated uptake of residues from the soil. Total residue levels in wheat and radish crops were similar for the plant-back intervals 29 and 120 days, but had significantly dropped in the crops planted after 365 days. At the 120 days plant-back interval the TRR in the mature edible crop parts reached 0.03 mg/kg in radish roots and 0.44 in wheat grain and was comparable to the levels found in the non-edible crop parts, i.e. in radish tops (0.04 mg/kg) and in wheat straw (0.36 mg/kg). In lettuce, however no total residues above 0.01 mg/kg were found at all three plant-back intervals.

On characterisation of the extractable radioactivity one component was identified in the crops at harvest as mepiquat, however with one exception (wheat chaff, 120 days) the levels were all below 0.01 mg/kg. Two polar metabolites were isolated, which individually were present at levels of less than 0.05 mg/kg in the crops, and thus were not further identified. The remaining extractable radioactivity was probably associated with metabolites (free, conjugated and incorporated) resulting from the fragmentation of the ring. The unextractable radioactivity in the crops accounted for less than 0.05 mg/kg and was probably associated with fragments of the ring that had been incorporated into natural plant products.

No rotational crop residue trial data was submitted. Though there was enrichment to significant levels of total radioactivity in the edible part of rotated crops, mepiquat *per se* was not found to be present at levels greater than 0.01 mg/kg. Moreover, in the rotational crop metabolism study the application was made to bare soil and does not reflect the conditions in practice, i.e. the interception by cereals at GS 31 to GS 49 (70% to 90% of applied substance).

Therefore it is not expected that residues above the LOQ of the analytical method for monitoring (0.05 mg/kg) will occur in rotational crops in practice.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

The metabolism and distribution in animals was investigated in lactating goats and chickens, using ring labelled ^{14}C- mepiquat chloride.

For lactating goats dosed at a rate of *ca* 20 mg/kg bw the majority of the administered radioactivity was excreted, mainly with urine and faeces (76%) and less than 0.1% in the milk. Additional 22% was assumed to be present in the gastrointestinal tract due to the short period between the last dose and sacrifice. Only 2% was recovered in the tissues.

On extraction and characterisation one major component was identified in the milk and tissues as mepiquat, representing 78-94% (milk 44%) of the total radioactivity in the milk and tissues. Several other metabolites were identified, plus several unknowns, which individually were present at levels of at or less than 0.1 mg/kg, with the exception of methyl piperidine which was present at a level of 0.5 mg/kg in kidney and 4-hydroxy-mepiquat which was present at a level of 6.9 mg/kg in liver. On further characterisation of the milk 53% of the total radioactivity was found to be associated with proteins; fats and carbohydrates, indicating the fragmentation of the ring and the natural incorporation of these fragments into proteins, fats and carbohydrates.

For chickens dosed at a rate of *ca* 20 mg/kg bw the majority, around 90% of administered radioactivity was recovered in the excreta; and individually less than 0.1% were present in the eggs and tissues. Among the tissues analysed, kidney (2.8 mg/kg), liver (1.3 mg/kg) and eggs (1.3 mg/kg) had the highest residue levels. Levels in fat and skin (0.8 mg/kg) and muscle (0.3 mg/kg) were lower. After dosing for 6 consecutive days a plateau was not reached in the eggs. The tissue to plasma radioactivity concentration ratio indicated greater tendency for short-term bioaccumulation in kidney, liver and eggs.

On characterisation of the extractable radioactivity one major component was identified in the excreta, eggs and tissues as mepiquat, representing 70-99% of the total radioactivity. In extracts of skin and muscle the metabolite methyl piperidine was found up to 9% of the TRR and in addition several minor metabolites, which individually were present at low levels and therefore not further identified.

None of the three metabolites identified in the animal products were identified in the rat metabolism studies. However, methyl piperidine and piperidine were only present at levels less than 10% TRR (up to 0.51 mg/kg) in studies carried out at highly exaggerated rates. Therefore, upon realistic exposure of livestock to mepiquat residues in feed no quantifiable levels of these metabolites are expected to be present in animal matrices. In the case of 4-hydroxy-mepiquat-chloride, however, significant levels were found in ruminant liver (40% TRR, up to 6.9 mg/kg), and therefore positive residues of this metabolite (exceeding the LOQ) may result in liver.

According to the meeting of experts in toxicology (PRAPeR 29) the metabolite 4-hydroxy-mepiquat-chloride should be considered as having similar mammalian toxicity to mepiquat-chloride.

Based on the data and information available the experts in PRAPeR 30 concluded that residues in animal products should be defined as sum of mepiquat, 4-hydroxy-mepiquat-chloride and their salts,

expressed as mepiquat chloride for risk assessment and as sum of mepiquat and its salts, expressed as mepiquat chloride for monitoring purposes.

Animal transfer studies were carried out on dairy cattle dosed at three different rates corresponding to 0.4, 2 and 6 mg/kg bw per day and on laying hens dosed at rates of 0.09, 0.44 and 1.3 mg/kg bw per day. Mepiquat was the only residue analysed for in the study and the results were expressed as mepiquat chloride.
For dairy cattle, positive residues were found in milk and tissues, with the highest residues in liver and kidney. A plateau was reached in milk after 4 days.
For hens, positive residues above the LOQ were only found in eggs from the highest dose group, reaching a plateau after 7 days.
Currently the maximum livestock dietary burden cannot be estimated due to incomplete residue trial data supporting the cGAP for the notified use in cereals. Thus the exact dose level to assess the residue levels that may occur in food of animal origin cannot be determined at the moment, the level is however likely to approximately correspond to the lowest dose level administered in the animal transfer studies.
As only mepiquat residues were analysed in the animal matrices but the residue definition for risk assessment includes the 4-hydroxy mepiquat metabolite (mainly relevant in ruminants), the experts in PRAPeR 30 identified a data gap for the applicant to submit a proposal for conversion factors for risk assessment of residues in animal matrices based on the existing data on ruminants or, if necessary, further information for the setting of such conversion factors.

Currently the consumer exposure assessment to potential residues in food of animal origin cannot be concluded nor can MRLs for animal matrices be proposed.

3.3. CONSUMER RISK ASSESSMENT

The experts in residues (PRAPeR 30) concluded that currently the consumer risk assessment **cannot be finalised**. The experts identified that further data and information is necessary to assess the levels of the relevant residues in cereals and in food of animal origin, in order to estimate consumer exposure and to establish MRLs.

In a provisional assessment (revised addendum 7 of January 2008 and RMS comments on EFSA draft conclusion of March 2008 – both not peer reviewed) based on the barley residue data only, the chronic dietary intake is well below (less than 6%) the proposed ADI for mepiquat-chloride of 0.2mg/kg bw/day. The estimate uses consumption data for barley and animal products from the WHO GEMS/Food European diet, assuming residue levels in barley grain of 2 mg/kg and residues in food of animal origin at levels of 0.05 mg/kg.
Likewise, the acute exposure is not expected to exceed the respective toxicological reference value (ARfD) for mepiquat-chloride of 0.3 mg/kg bw/day. In a provisional estimate with UK consumption data the RMS indicated that the NESTIs for adults, children, toddlers, infants, vegetarians and the elderly are all 3% or less of the ARfD.

However, a precise risk assessment regarding the notified representative use on cereals is only possible when the identified data gaps are filled.

It is moreover noted that the consumer risk assessment cannot be finalised with regard to the use of the formulated product containing besides mepiquat also the active substance ethephon. Ethephon residues arising from the notified use were not evaluated.

3.4. PROPOSED MRLS

The experts in the meeting PRAPeR 30 concluded that insufficient data is currently available to propose MRLs for the notified representative use on cereals and to finalise MRL proposals and conversion factors for food of animal origin.

However, sufficient data has been submitted that would allow for an MRL proposal of 2 mg/kg for barley grain. If, deviating from the notified use on cereals, a use of mepiquat-chloride on barley only were considered, the following MRL proposals for food of animal origin made by the RMS could be applicable: Milk, meat, fat and eggs 0.05 mg/kg; kidney and liver 0.1 mg/kg. It is however noted that such modification of the notified representative use was not discussed in the meeting of experts, and thus these MRL proposals should not be considered peer reviewed.

It was also noted by the experts that if it were agreed on management level that the residue definition for monitoring/ MRL setting should be mepiquat and not the variant mepiquat chloride, a recalculation of all results used for the MRL proposals would be necessary.

4. Environmental fate and behaviour

Mepiquat-chloride was discussed at the PRAPeR experts' meeting (PRAPeR 27) in July 2007, on the basis of the DAR and the addendum to Vol 3 rev. 1 (June 2007). In line with the toxicity endpoints expressed as mepiquat-chloride, all the environmental exposure concentrations were calculated for mepiquat-chloride.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Degradation of mepiquat-chloride under aerobic dark conditions (20ºC and 40% MWHC) was investigated in 4 soils (pH 5.8-7.5; organic carbon content 1.0-2.1%; clay content 1.5-11.2%). One of the soils was tested also at 10 ºC.

The major degradation pathway of mepiquat-chloride in soil is formation of CO_2 (43.1-69.7% AR after 120d). The non-extractable residues amounted to values of 15.8-43.7% AR at the end of incubation period. No significant metabolites (> 10% AR) were identified in any soil at any time point.

At lower temperature the degradation of mepiquat-chloride is slowed down, reaching a mineralisation rate of 17.8% AR and formation of non-extractable residues of 31.3% AR.
A laboratory soil photolysis study is available. There were no significant differences between the levels of mepiquat-chloride remaining in dark and irradiated samples after 30 d, therefore the test substance was photolytically stable. A photolytic half-life could not therefore be determined.

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

Degradation rate of mepiquat-chloride was investigated in the same soils used to establish the route of degradation, including a supplementary soil tested, for which a complete material balance was not available. Additionally, degradation in soil under dark aerobic conditions (25ºC and 75% FC at 1/3 bar) was investigated in a radiolabelled study at a lower application rate (0.265 µg/g soil ≈ 200 g a.s./ha) with one soil (pH 5.7; clay 10% and organic carbon content 0.9%). Single first order DT_{50} values were estimated to be 6-40 days. After normalisation to field capacity soil moisture content (-10kPs) and 20ºC was 5-37 days.
Field dissipation studies were not required for mepiquat-chloride since aerobic degradation in the laboratory resulted in half-lives below the trigger of 60 days.

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

Three batch adsorption/desorption studies are available for mepiquat-chloride on 9 soils (pH 6.1-7.3; organic carbon content 0.5-2.7%) in total. In one of the study, the adsorption and desorption isotherms were evaluated at two different temperatures (18ºC and 22ºC) on 3 soils. Based on the data available (n=12) mepiquat-chloride can be characterized as having slight to high mobility in soil, with reliable K_f values of 1.69-25 mL/g and the respective K_foc values in the range 67-4833 mL/g (1/n = 0.914-0.991). No correlations between the K_f value and soil parameters were statistically significant.
A laboratory aged column leaching study was performed with aged (30 days at 20ºC in the dark) residues of mepiquat-chloride in one soil (sand soil, organic carbon 0.5%, pH in $CaCl_2$ 5.6). The total radioactivity found in the percolates of each experiment did not exceed 0.08% of the radioactivity applied to the column. The radioactive residue in the soil segments was predominantly distributed in the top 24 cm of soil. The majority of radioactivity was present as unextracted soil residues.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

The octanol:water partition coefficient ($logP_{ow}$) of mepiquat-chloride is -3.45 in deionised water. Mepiquat-chloride solubility in water is > 500g/L and it is expected to be completely dissociated in aqueous solutions (forming a cation and a chloride ion).
The hydrolysis data indicated that mepiquat-chloride is stable to hydrolysis. There was no significant degradation at pH 3 to pH 9 at 25ºC). Therefore, hydrolysis is not considered a route of dissipation.

In an aqueous photolysis study, mepiquat-chloride was stable under non-sensitised conditions and in the presence of a photosensitiser.

The available study on the ready biodegradability (OECD 301A, DOC Die Away Test) of mepiquat chloride was discussed at the meeting of experts. Based on the additional information provided in Addendum 1 it was agreed that the study is considered valid and the classification for mepiquat-chloride as "readily biodegradable" was confirmed.

The degradation of mepiquat-chloride under aerobic aquatic conditions was investigated in two different natural systems of water and sediment. The results showed that mepiquat-chloride dissipated quickly from the water phase by partitioning to the sediment. Peak partitioning of mepiquat-chloride to the sediment was measured 14 to 30 days after dosing at a maximum of 56.2% AR. Mineralisation was significant and by the termination of the study carbon dioxide amounted to 61.7-65.8% AR. No significant quantities of metabolites were detected. First order DT_{50} values for mepiquat-chloride for the whole system were 32 to 33 days and 22 and 25 days in the sediment.

Predicted environmental concentrations in surface water for mepiquat-chloride were calculated following the tiered approach recommended by the FOCUS working group. PECsw and PECsed calculations with Steps 2 model were based on the average Koc value of 890 L/kg and assuming a very worst case $DT_{50\ water}$ value of 999 days (no degradation in water assumed).

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

The leaching model FOCUS PELMO 3.3.2 was used to investigate the potential for contamination of groundwater by mepiquat-chloride. The active ingredient was assumed to be applied at GS 31-49 to cereals, with a crop interception of 70% for elongation stage for winter cereals. Since no dependence of the sorption of mepiquat-chloride on the organic carbon content was found, the K_f rather than the Koc value was used in the modelling. Scenario specific K_f and 1/n values were selected based on similarities between the modelling scenario soils and the soils used in the batch equilibrium adsorption studies. In Addendum 1, the RMS repeated the exposure assessment using the median $K_f$oc of 890 mL/g derived from the 12 acceptable soils in the DAR and a 1/n value of 1 as a simple worst case. In both simulations (scenario specific K_f and median $K_f$oc of 890 mL/g) the 80th percentile annual average concentrations in leachate leaving the top 1 m soil layer were predicted to be < 0.001 µg/L for all FOCUS scenarios pertinent to use on winter cereals.

4.3. FATE AND BEHAVIOUR IN AIR

Mepiquat-chloride has a low vapour pressure of <1 x 10^{-8} Pa at 20°C and the Henry's Law constant was calculated to be 3.0 x 10^{-12} kPa.m^3/mol. Therefore it is essentially non-volatile and there is little potential for volatilisation from either soil or plant surfaces. Consequently, air is not a likely route of environmental contamination.

5. Ecotoxicology

Mepiquat-chloride was discussed at the experts' meeting for ecotoxicology (PRAPeR) in July 2007.

5.1. RISK TO TERRESTRIAL VERTEBRATES

Birds and mammals may be exposed to mepiquat-chloride by intake of insects present in the treated crop. Since mepiquat-chloride is to be applied after BBCH growth stage 31 the crop itself is assumed to be past the stage were it is attractive as food.

The risk to generic species, representing insectivorous birds and mammals was assessed according to SANCO/ 4145/2000 for the use of 0.7625 kg a.s./ha. The acute and short-term TER values for birds are well above the Annex VI triggers in the first tier assessment, hence indicating a low risk. The long-term TER value for birds is 4.4 and thus below the Annex VI trigger of 5. For mammals, both the acute and long-term TER values are well above the triggers, hence the risk to mammals is considered as low.

A new long-term (reproduction) study with birds was presented in an addendum (June 2007) together with a new risk assessment for insectivorous birds based on yellowhammer (*Emberiza citronella*) as a focal species. The experts agreed to use the endpoint from the new study with Japanese quail (*Coturnix coturnix* Japonica). The refinement of PT and PD were accepted by the experts. The refined long-term TER was calculated to be 8.53.

The risk to birds from the second active substance (ethephon) in the representative formulation "Terpal" was not considered in the original risk assessment. No toxicity endpoints for the formulation were available for birds. The applicant submitted a position paper stating that the toxicity of the formulation to birds would not be significantly higher than for mepiquat alone based on test results observed for mammals. The reliability of the argumentation was considered as uncertain by the RMS. The RMS presented in the addendum an acute risk assessment based on additive toxicity according to the formula of Finney. The resulting acute TERs were still above the trigger and the risk to birds was considered as sufficiently addressed. The experts agreed that the risk to birds is sufficiently addressed for the formulated product and that no new studies are necessary.

Since the $\log P_{ow}$ for mepiquat-chloride is -3.45, the potential for bioaccumulation is considered as negligible and no assessment of exposure via consumption of earthworms from contaminated soil or fish from contaminated surface water is necessary.

A risk assessment for the uptake of contaminated drinking water according to SANCO/ 4145/2000 was included in the addendum. The TERs of >7.3 (birds) and 2.2 (mammals) were below the trigger of 10. No agreement was reached in the expert meeting on the relevance of this exposure route for the suggested use in cereals. It was proposed by the experts that this point should be left open to be considered at MSs level after Annex I inclusion since the relevance of this exposure scenario may

depend on the local weather conditions and the landscape structure (availability of alternative drinking water sources).

5.2. RISK TO AQUATIC ORGANISMS

The lowest acute toxicity endpoint was the E_bC_{50} of 2.6 mg/L for *Lemna gibba* The proposed classification for mepiquat-chloride is therefore 'Toxic to aquatic organisms' (R51). Acute studies with the formulation do not indicate a higher toxicity to aquatic organisms compared to the technical material.

Based on FOCUS step 1 PEC_{sw} calculations with an application rate of 0.7625 kg mepiquat-chloride per hectare the TER value for *Lemna* sp, the most sensitive species is 21 which is above the Annex VI trigger of 10. Also the long-term risk to fish and invertebrates is considered low.

Mepiquat-chloride partitions into sediment, and was found in amounts of 48-56% of applied in the water/sediment studies. However, since the NOEC for *Daphnia* is 12.5 mg/L, which is >0.1 mg/L, a study with sediment dwelling organisms is not required according to SANCO/3268/2001.

The log P_{ow} for mepiquat-chloride is <3 and therefore the potential for bioconcentration is considered as low. No major metabolites (≥10%) were detected in the water/sediment study.

5.3. RISK TO BEES

The formulation BAS 098 00W is to be applied to cereals at a time when aphids may be present and producing honeydew. Bee s may also be attracted to flowering weeds in the treated field. Oral and contact toxicity studies are available with mepiquat-chloride and the formulation. Comparison of the end point values from these studies with the application rate gives HQ values well below the Annex VI trigger of 50 for mepiquat-chloride as well as the formulation. Hence the risk to bees is considered to be low.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Laboratory studies with the two standard species *Typhlodromus pyri* and *Aphidius rhopalosiphi* are available from which LR_{50} values could be obtained for mepiquat-chloride. When compared to the proposed application rate the in-field HQ values are <0.5 and <0.56 respectively. Both HQ values are below the ESCORT II trigger of 2 and consequently the in-field and off-field risk is considered to be low. Also the HQ-value based on the LR_{50} from a study with *T. pyri* and the formulation is below the trigger (TER=0.67). Extended laboratory studies with *A. rhopalosiphi* and *T. pyri* with the formulation on natural substrate did not show any effects on mortality above 50% and no significant effects on reproduction. Further data from laboratory studies on inert substrate with the leaf dwelling *Chrysoperla carnea* and the soil dwelling *Aleochara bilineata* indicate that the risk to non-target arthropods is low.

5.5. RISK TO EARTHWORMS

Acute toxicity studies with earthworms are available with mepiquat-chloride and the formulation BAS 098 00W. TER values calculated based on the results of these studies and initial PEC_{soil} are 1048 and 274 for mepiquat-chloride and the formulation respectively. Since this is well above the Annex VI trigger of 10, the acute risk is considered to be low. The DT_{90} for mepiquat-chloride in soil is 133 days. According to the "Guidance Document on Terrestrial Ecotoxicology" (SANCO/10329/2002) the decision whether chronic studies are required should be taken on a case by case basis if the soil DT_{90} is between 100 and 365 days. The RMS presented in the DAR an assessment according to the EPPO scheme for soil organisms and functions[2]. The ratio of the acute LC_{50}/NOEC was <10 and the ratio of PECsoil/NOEC was <0.1 suggesting a low chronic risk. The product is applied only once per year. Overall it is concluded that the long-term risk to earthworms is regarded as low.

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

No studies on other soil non-target macro-organisms are available. Since the HQ values for the two standard non-target arthropods are below 2 and no effects were observed on the soil dwelling *Aleochara bilineata* no studies are required although DT_{90} in soil is longer than 100 days.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects on soil respiration and nitrification were tested with a formulation containing mepiquat-chloride only and with the formulation BAS 098 00W. No deviation from the control >25% at 100 days was observed.

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

Seedling emergence and vegetative vigour was tested on 4 dicotyledonous (*Daucus caota*, *Linum usitatissium, Brassica napus, Pisum sativum*) and 2 monocotolydonous (*Avena sativa*, *Allium cepa*) species. ER_{50} was >3000 mg product/ha for both emergence and vegetative vigour. Comparing the ER_{50} with the dose rate corresponding to 2.77% drift at 1m from the field gives a TER of 43.3 which is above the trigger of 5 proposed in the "Guidance Document on Terrestrial Ecotoxicology" (SANCO/10329/2002).

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Data from a test with mepiquat-chloride on effects on activated sludge respiration rate are available and indicate that the risk to biological methods of sewage treatment plants is low.

[2] Normes OEPP, EPPO Standards, Environmental risk assessment scheme for plant protection products. OEPP/EPPO Bulletin 33, 147-149

6. Residue definitions

Soil

Definitions for risk assessment: mepiquat-chloride

Definitions for monitoring: sum of mepiquat-chloride and its salt expressed as mepiquat chloride

Water

Ground water

Definitions for exposure assessment: mepiquat-chloride

Definitions for monitoring: sum of mepiquat-chloride and its salt expressed as mepiquat chloride

Surface water

Definitions for risk assessment: mepiquat-chloride

Definitions for monitoring: sum of mepiquat-chloride and its salt expressed as mepiquat chloride

Air

Definitions for risk assessment: mepiquat-chloride

Definitions for monitoring: sum of mepiquat-chloride and its salt expressed as mepiquat chloride

Food of plant origin

Definitions for risk assessment: sum of mepiquat and its salts, expressed as mepiquat chloride

Definitions for monitoring: sum of mepiquat and its salts, expressed as mepiquat chloride

Food of animal origin

Definitions for risk assessment: mepiquat, 4-hydroxy-mepiquat-chloride and their salts, expressed as mepiquat chloride

Definitions for monitoring: sum of mepiquat and its salts, expressed as mepiquat chloride

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
Mepiquat-chloride	Moderate to medium persistence First order $DT_{50\ lab}$ = 6-40 d (20-25°C, 40% MWHC or 75% FC at 1/3 bar)	The risk to soil dwelling organisms was assessed as low.

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 relevance**
Mepiquat-chloride	Slight to high mobility (Kfoc = 67-4833 mL/g)	FOCUS PELMO 3.3.2: no	Yes	Yes	The risk to aquatic organisms in surface water was assessed as low.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Mepiquat-chloride	Mepiquat-chloride is toxic to aquatic organisms. The risk to aquatic organisms was assessed as low.

Air

Compound (name and/or code)	Toxicology
Mepiquat-chloride	Proposed classification as R20 Harmful by inhalation

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

- Validation data for the HPLC-MS/MS method in line with SANCO 825/00 for milk, egg, fat and muscle. (relevant for all representative uses evaluated, date of submission unknown, data gap identified by experts of PRAPeR 31 meeting, October 2007; refer to chapter 1)
- 8 additional residue trials are required for wheat with application at GS 49. If significant differences are noted between the wheat and the available barley trials, further data may be required for the individual cereals (relevant for all representative uses evaluated, data gap identified by the meeting of experts PRAPeR 30 in July 2007; submission date proposed by the notifier unknown; refer to point 3.1.1)
- A proposal for conversion factors for risk assessment of residues in animal matrices based on the existing data on ruminants or, if necessary, further information for the setting of such conversion factors is required (relevant for all representative uses evaluated, data gap identified by the meeting of experts PRAPeR 30 in July 2007; submission date proposed by the notifier unknown; refer to point 3.2)

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 foliar spraying with conventional spraying devices for stem stabilisation on barley, oats, wheat and rye, up to growth stage of BBCH 31-49, in northern EU countries, at a single application at a maximum application rate of 762.5 g a.s./ha (mepiquat chloride).

The representative formulated product for the evaluation was “Terpal” (BAS 098 00 W), a soluble concentrate (SL) containing 305 g/l mepiquat-chloride and 155g/l ethephon, registered in several EU member states.

Adequate analytical methods are available to monitor all compounds given in the respective residue definitions in food/feed of plant and animal origin and environmental matrices, however data gaps were identified for validation data for the residue method for milk, egg, fat and muscle.
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.

In mammalian toxicity tests, mepiquat-chloride is harmful to rats after oral exposure and is proposed for classification with R22 “Harmful if swallowed” (LD50 464 mg/kg bw, equivalent 270 mg/kg bw mepiquat). The acute dermal LD50 of mepiquat-chloride in rats is >2000 mg/kg bw; the acute inhalation LC50 in the rat for mepiquat-chloride was approximately 4.89 mg/l (equivalent to 2.84 mg/L mepiquat), the maximum attainable concentration under the experimental conditions and thus it

is proposed for classification with R20, Harmful by inhalation. Mepiquat-chloride is not a skin or eye irritant, nor sensitizing. The relevant short term toxicity NOAEL is an overall NOAEL of 30.5 mg/kg bw/day from 3- and 12-month study in dog that showed salivation and some mortalities, vacuolisation of the kidney and increased accumulation of siderin in the liver and spleen, whose mechanism and toxicological significance is unclear. Mepiquat-chloride does not show any genotoxic or clastogenic potential in a range of *in vitro* and *in vivo* studies. Mepiquat-chloride does not show any carcinogenic potential either in rats or mice. The relevant NOAEL in long term toxicity studies in rat is 200 mg/kg bw/day. Mepiquat-chloride does not show any reproductive or developmental toxicity potential: the relevant NOAEL for maternal, reproductive and offspring toxicity is 320 mg/kg bw/day based on reduction in viability and lactation indices, body weight and the impaired morphological development in the offspring; in the developmental toxicity study in rats the NOAEL for maternal toxicity is 150 mg/kg bw/day based on clinical signs of toxicity and impaired body weight gain at 300 mg/kg bw/day and for foetotoxicity and teratogenicity 300 mg/kg bw/day based on the absence of any other signs of toxicity at the highest test dose in the study. In a developmental neurotoxicity study, administration of mepiquat resulted in acute lethality for gavaged pups. The ADI is 0.2 mg/kg bw/day based on the NOAEL of 19.9 mg/kg bw/day from the 12-month dietary study in dogs; the AOEL is 0.3 mg/kg bw/day based on the NOAEL of 30.5 mg/kg bw/day from the 90-day study in dogs; the ARfD of 0.3 mg/kg bw is based on the NOAEL of 30 mg/kg bw/day obtained in the developmental neurotoxicity study. The applied SF is 100. Estimated operator exposure with the German model indicate for operators not wearing PPE levels below the AOEL (10 %) as well as using UK POEM (70% of the AOEL). Predicted bystander exposure is <1% of the short term systemic AOEL. Estimates of exposure to mepiquat-chloride using data for re-entry exposure contained in the EUROPOEM database indicate exposure levels below the AOEL (3.5%).

The metabolism of mepiquat chloride was investigated in wheat, barley, cotton and grapes. The major component in the crops at harvest was unmetabolised mepiquat. Though rotational crops data were not triggered by the residue behaviour of mepiquat chloride in soil, a metabolism study in rotational crops with radio-labelled substance was submitted. The data indicate that in practice residues above the limit of quantification of the analytical method are not expected to occur in succeeding and rotational crops.

Currently, only the use of mepiquat chloride on barley would be supported by a sufficient number of valid residue trial data while the notified representative use is on cereals in general. Therefore a data gap for further residue trials was identified.

Animal metabolism studies with ruminants and poultry are available to establish the nature of residues in food of animal origin. Since insufficient data is available to assess the magnitude of residues in cereal grain and straw, the livestock exposure assessment cannot be finalised. Moreover, the residue analysed in the livestock feeding studies does not correspond to the proposed animal residue definition for risk assessment, and further data and information is needed to establish reliable transfer factors of residues in food of animal origin and conversion factors for monitoring.

Therefore the meeting of experts concluded that the consumer risk assessment and MRL proposals cannot be finalised. If deviating from the notified use on cereals a use of mepiquat-chloride on barley

only is considered, consumer exposure is expected to be well below the toxicological reference values for mepiquat-chloride and MRLs could be proposed.

The information on fate and behaviour in the environment is sufficient to carry out an appropriate environmental exposure assessment at EU level. For the applied for intended uses, the potential for groundwater exposure above the drinking water limit of 0.1 µg/L is low.

The risk to birds and mammals from uptake of contaminated food was assessed as low. The long-term risk to insectivorous birds needed refinement. The suggested refinement based on yellowhammer (*Emberiza citronella*) as a focal species and PT and PD values were accepted by the experts.
A risk assessment for the uptake of contaminated drinking water according to SANCO/ 4145/2000 resulted in acute TERs of >7.3 (birds) and 2.2 (mammals) which are below the trigger of 10. No agreement was reached in the expert meeting on the relevance of this exposure route for the suggested use in cereals. It was proposed by the experts that this point should be left open to be considered at MSs level after Annex I inclusion since the relevance of this exposure scenario may depend on the local weather conditions and the landscape structure (availability of alternative drinking water sources). The most sensitive aquatic organism tested and driving the aquatic risk assessment was *Lemna gibba*. The TERs were above the trigger of 10 with FOCUS step 1 PEC_{sw} indicating a low risk. Mepiquat-chloride partitions into sediment, and was found in amounts of 48-56% of applied in the water/sediment studies. However, since the NOEC for *Daphnia* is 12.5 mg/L, which is >0.1 mg/L, a study with sediment dwelling organisms is not required according to SANCO/3268/2001. The log P_{ow} for mepiquat-chloride is <3 and therefore the potential for bioconcentration is considered as low. No major metabolites (≥10%) were detected in the water/sediment study. The risk to bees, other non-target arthropods, earthworms, soil non-target micro-organisms and biological methods of sewage treatment was assessed as low.

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

- None

Critical areas of concern

- The operator, worker and bystander risk assessment should be regarded as inconclusive because Terpal is a combi product (mepiquat and ethephon), and the influence of ethephon on the risk has not been investigated.
- The consumer risk assessment cannot be finalised for the notified use comprising the broad category of cereal crops due to lack of data. Moreover, consumer risk was not assessed with regard to the use of the formulated product, containing besides mepiquat also the active substance ethephon.

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

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

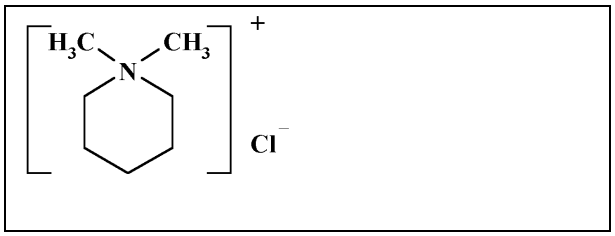
Appendix 1.1Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

Active substance (ISO Common Name) ‡	Mepiquat (unless stated otherwise, the following data relate to the variant mepiquat chloride).
Function (*e.g.* fungicide)	Plant growth regulator
Rapporteur Member State	UK
Co-rapporteur Member State	Not applicable

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	1,1-dimethylpiperidinium chloride (mepiquat chloride)
Chemical name (CA) ‡	1,1-dimethylpiperidinium chloride (mepiquat chloride)
CIPAC No ‡	440.302 (mepiquat chloride) 440 (mepiquat)
CAS No ‡	24307-26-4 (mepiquat chloride) 15302-91-7 (mepiquat)
EC No (EINECS or ELINCS) ‡	246-147-6 (mepiquat chloride)
FAO Specification (including year of publication) ‡	None
Minimum purity of the active substance as manufactured ‡	615-665 g/l in the technical concentrate (TK)*****, corresponding to a minimum purity in the theoretically dry technical material (TC) of 990 g/kg.
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	$C_7H_{16}ClN$ (mepiquat chloride) $C_7H_{16}N$ (mepiquat)
Molecular mass ‡	149.7
Structural formula ‡	Mepiquat chloride

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



***** Mepiquat chloride is very hygroscopic and therefore the dry technical material (TC) is not isolated during production, but is diluted with water to give an aqueous technical concentrate (TK) containing ~60% mepiquat chloride.

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

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	No melting occurs up to 300°C (99.3%)
Boiling point (state purity) ‡	No boiling up to the decomposition temperature of 320°C (99.3%)
Temperature of decomposition (state purity)	320°C. (99.3%)
Appearance (state purity) ‡	Odourless white crystalline solid (99.3%) Odourless light yellow liquid (59.9% TK)
Vapour pressure (state temperature, state purity) ‡	$<10^{-8}$ Pa at 20°C and 25°C (99.3%)
Henry's law constant ‡	$<2.994 \times 10^{-12}$ Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	>50 %w/w (99.5%) (temperature and pH not reported)
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility in g/l at 20°C methanol: 344 toluene: <0.01 n-octanol: 9.96 n-heptane: <0.01 ethylacetate: <0.01 dichloromethane: 0.51 acetonitrile 2.78 acetone: 0.02 (99.3%)
Surface tension ‡ (state concentration and temperature, state purity)	47.4 mN/m at 20°C (1 %w/w)(99.3%)
Partition co-efficient ‡ (state temperature, pH and purity)	log $P_{O/W}$ = -3.45 at 20 °C (deionised water (99.3%) log $P_{O/W}$ = -3.20 at 20 °C (pH 4 (99.3%) log $P_{O/W}$ = -3.55 at 20 °C (pH 7 (99.3%) log $P_{O/W}$ = -3.14 at 20 °C (pH 10 (99.3%)
Dissociation constant (state purity) ‡	Mepiquat chloride completely dissociates in aqueous solutions and therefore has no dissociation constant. Protonation of the resulting mepiquat cation is impossible and deprotonation by an extremely strong alkali would trigger decomposition by Hofmann degradation, therefore it has no dissociation constant. The protonation/deprotonation reaction of the chloride cation has a pKa of -7 (Cotton F. A., Wilkinson G. et al., Advanced Inorganic Chemistry 1999, pp. 62, 63). The extremely high proton concentrations required for this have only theoretical significance.

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

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	No significant UV-visible absorption from 200 to 750 nm, at pH 1, 6 or 13. The molar extinction coefficient of mepiquat chloride at 295 nm is 0.0974 cm^2 $mMol^{-1}$. (99.3%)
Flammability ‡ (state purity)	Not flammable (TK)
Explosive properties ‡ (state purity)	Not explosive (TK)
Oxidising properties ‡ (state purity)	Not oxidising (TK)

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

Appendix 1 – List of endpoints

Summary of representative uses evaluated (*mepiquat chloride*)*

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 (for explanation see the text in front of this section)			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)	kg as/hL min – max (l)	water L/ha min – max	kg as/ha min – max (l)		
Cereals	Belgium, Denmark, Finland France, Ireland, Luxembourg, Sweden, United Kingdom	Terpal Terpal Terpal Terpal Terpal Terpal Terpal Terpal	F	Stem stabilisation	SL	**305**** 155***	SP	31 – 49	1	-	**0.127 - 0.508**** 0.065 - 0.258***	150 - 600	**0.7625**** 0.3875***	*[2]*	*[1]*

There are more products/uses available or under preparation which will be supported on the national level.

* splitting not particularly displayed here - (*Max 0.458 (ww&wb): Maximum 2 litres/product/hectare/crop (0.610 kg ai/ha/crop) must not be exceeded when applying split dose applications).

** mepiquat chloride

*** ethephon

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

[1] Residue trial data base for cereals incomplete, consumer risk assessment and MRL proposal for the use in the broad category of cereals cannot be finalised. Complete data is available only to support a use in barley; and based on this data no risk to consumers is expected.

[2] covered by conditions of use

‡ End point identified by the 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)	CIPAC method 440/TK/M/3
Impurities in technical a.s. (analytical technique)	Aliquots of technical material were dissolved in water and analysed by indirect photometric chromatography with UV detection at 254 nm (isocratic elution using a PRP X200 analytical column and water:methanol [8:2 v/v] containing benzyltrimethyl ammonium chloride mobile phase).
Plant protection product (analytical technique)	Mepiquat chloride - An aliquot of the formulation was diluted with water and analysed by ion exchange HPLC with conductivity detection (isocratic elution using a 250mm x 4.6mm Zorbax 300-SCX analytical column and water:acetone:0.5 mol/l ethylene diamine:0.5 mol/l oxalic acid [850:150:5:7 v/v/v/v] mobile phase). Ethephon - An aliquot of the formulation was diluted with water and adjusted to pH 9.6 by the addition of potassium hydroxide solution. The mixture was boiled under reflux for 30 minutes. The cooled mixture was titrated to a pH of 9.6 with a standardised solution of 0.1 mol/l potassium hydroxide and the titer volume of potassium hydroxide was used to determine the content of ethephon in the sample.

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		The sum of mepiquat and its salts expressed as mepiquat chloride.
Food of animal origin		The sum of mepiquat and its salts expressed as mepiquat chloride.
Soil		The sum of mepiquat and its salts expressed as mepiquat chloride.
Water	surface	The sum of mepiquat and its salts expressed as mepiquat chloride.
	drinking/ground	The sum of mepiquat and its salts expressed as mepiquat chloride.
Air		The sum of mepiquat and its salts expressed as mepiquat chloride.

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

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Method 505/0 - Samples were extracted with water/methanol/2N HCl (65:30:5 v/v/v). Extracts were cleaned-up by solid phase extraction using Al2O3 as sorbent and determined by reverse phase HPLC-MS-MS (gradient elution using Alltima C18 or Aquasil C18 Thermohypersil-Keystone analytical column and water/formic acid/methanol mobile phase). Ion transitions m/z 114 → 98 and m/z 114→ 58 were monitored, and fragment ion m/z 98 was used for quantification. The proposed HPLC-MS-MS method is highly specific and therefore a separate confirmatory method is not required. (LOQ 0.05 mg/kg in wheat forage, barley grain, maize straw, grape, apple, oilseed rape seed, wheat grain and various processing products of wheat and barley).
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Method 505/0 - Samples were extracted with water/methanol/2N HCl (65:30:5 v/v/v). Extracts were cleaned-up by solid phase extraction using Al2O3 as sorbent and determined by reverse phase HPLC-MS-MS (gradient elution using Spherisorb ODS1 analytical column and ammonium for,mate/water/acetonitrile/acetic acid/methanol mobile phase). Ion transitions m/z 114 → 98 and m/z 114→ 58 were monitored, both ions were suitable for quantification. The proposed HPLC-MS-MS method is highly specific and therefore a separate confirmatory method is not required. (LOQ 0.05 mg/kg in liver and kidney).

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

Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes) continued	Method 23 and its addendum dated 21/02/1979 – for the confirmation of residues in foodstuff of animal origin. Milk and Egg samples were extracted with methanol followed by 25% aqueous 0.5N HCl in methanol. Beef and chicken tissue samples were extracted with 0.125N HCl in methanol. Urine samples were diluted with methanol. All extracts were cleaned up on a cation exchange column, and mepiquat chloride was eluted from the column with 12.5% aqueous HCl solution. The acidic eluate was evaporated to dryness and reconstituted into water prior to liquid-liquid partition with dipicrylamine/dichloromethane solution. The dipicrylamine/dichloromethane phase was then extracted by liquid-liquid partition with 2M HCl solution. The combined aqueous phases were evaporated to complete dryness and transferred to a demethylation reaction vessel using 0.5N HCl in methanol. The methanol was subsequently removed by evaporation, after which mepiquat chloride was converted to N-methylpiperidine by reaction with a mixture of diethanolamine and hexamethylphosphoramide. The N-methylpiperidine was isolated with hexane. The hexane extract was then cleaned up with o-phenylene phosphorochloridite prior to analysis by GC-NPD (analytical column packed with Chromosorb 103). (LOQ 0.05 mg/kg)
Soil (analytical technique and LOQ)	Samples were extracted successively with solutions of sodium tetraphenyl borate (ion pairing reagent) in dichloromethane (0.2 mg/ml followed by 0.1 mg/ml) followed by pure dichloromethane. The combined extracts were filtered and partitioned into 2 M HCl. The HCl extracts were reduced to dryness then reconstituted with water and reduced to dryness again (to completely remove HCl) before being reconstituted with acetonitrile/methanol (95:5 v/v). The extracts were cleaned-up by solid phase extraction using Al_2O_3 as sorbent and determined by ion chromatography with suppressed conductivity detection (isocratic elution using a Hamilton PRP-1 analytical column and 2 mM 1-hexanesulphonic acid/ acetonitrile (95:5 v/v) mobile phase). A reversed phase HPLC-MS-MS method was used for confirmation. Ion transitions m/z 114 → 98 and m/z 114→ 58 were monitored, and fragment ion m/z 98 was used for quantification. (LOQ 0.01 mg/kg)

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

Water (analytical technique and LOQ)	Samples were cleaned up by liquid-liquid partition with dichloromethane. Sodium tetraphenylborate (ion pairing reagent) was then added to the samples and they were extracted twice by liquid-liquid partition with dichloromethane. The combined extracts were then partitioned into 2M HCl. The HCl extracts were reduced to dryness then reconstituted with water and reduced to dryness again (to completely remove HCl) before being reconstituted with acetonitrile/methanol (95:5 v/v). The extracts were cleaned-up by solid phase extraction using Al_2O_3 as sorbent and determined by ion chromatography with suppressed conductivity detection (isocratic elution using a Hamilton PRP-1 analytical column and 2 mM 1-hexanesulphonic acid/ acetonitrile (95:5 v/v) mobile phase). A reversed phase HPLC-MS-MS method was used for confirmation. Ion transitions m/z 114 → 98 and m/z 114→ 58 were monitored, and fragment ion m/z 98 was used for quantification. (LOQ 0.05 µg/kg)
Air (analytical technique and LOQ)	The adsorbers were extracted with water and diluted to a fixed volume prior to analysis by ion chromatography with conductivity detection (isocratic elution using a Hamilton PRP-1 analytical column and 2 mM 1-hexanesulphonic acid/ acetonitrile (95:5 v/v) mobile phase). A reversed phase HPLC-MS-MS method was used for confirmation, monitoring for ion transitions m/z 114 → 98 and m/z 114→ 58. (LOQ 0.016 mg/m^3)
Body fluids and tissues (analytical technique and LOQ)	Not required as mepiquat chloride is not classified as toxic or highly toxic.

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

	RMS/peer review proposal
Active substance	None.

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

Appendix 1.3 Impact on Human and Animal Health

All values in this section are reported as mepiquat chloride and may be expressed as mepiquat ion by multiplying by a factor of 0.77

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

Rate and extent of oral absorption ‡	Rapidly absorbed. Bioavailability after an oral dose of ≤ 12 mg/kg bw was approximately 85 %
Distribution ‡	Extensively distributed into organs and tissues. Peak levels in blood within 40 minutes after an oral dose
Potential for accumulation ‡	Low.
Rate and extent of excretion ‡	Rapidly eliminated mostly in urine, approximately 70 % was eliminated within 12 h after an oral dose. Excretion in both faeces and urine amounted to 80-90 % of the administered dose after one day and was mostly > 90 % after 2 days.
Metabolism in animals ‡	No evidence of metabolism was observed in rats. However, after a relatively large dose, conjugates of 4-hydroxymepiquat chloride were observed in liver and milk of lactating goats.
Toxicologically relevant compounds ‡ (animals and plants)	Parent mepiquat chloride
Toxicologically relevant compounds ‡ (environment)	Parent mepiquat chloride

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	464 mg/kg bw (270 mg ai/kg bw) for males and 200 – 464 mg/kg bw in females). Combined: 464 mg/kg bw (270 mg ai/kg bw). No clear sex differences. Classified with R22 Harmful if swallowed.	R22
Rat LD_{50} dermal ‡	> 2,000 mg/kg bw (test substance) = > 1,160 mg a.s./kg bw	
Rat LC_{50} inhalation ‡	> 4.89 mg/l (test substance) ≡ > 2.84 mg a.s./l at maximum attainable concentration. Mortalities (2/5 in males and 1/4 in females) suggests that at limit dose for classification of 5 mg/l mortality of >50% could be expected for males, hence proposal to classify with R20 Harmful by inhalation.	R20
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant	
Skin sensitisation ‡	Not sensitising to skin (Landsteiner-Draize method; includes a non-adjuvant intradermal induction exposure)	

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

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Impaired growth in rats, no effects in mice at ≤1000 mg asi/kg bw/day. In dogs clinical signs including salivation, mortality, vacuolisation of the kidney and increased accumulation of haemosiderin in the spleen.	
Relevant oral NOAEL ‡	30.5 mg/kg bw/day overall in dogs based on 3 and 12-month oral studies	
Relevant dermal NOAEL ‡	1000 mg/kg bw/day	
Relevant inhalation NOAEL ‡	Not relevant. Vapour pressure of <10-8 Pa at 20°C and 25°C, indicating that it is only very slightly volatile	

Genotoxicity ‡ (Annex IIA, point 5.4)

Overall, no genotoxic potential	

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

Target/critical effect ‡	Reduced body weight gain at high dose levels in rats and mice. In dogs increased salivation, mortality, vacuolisation of the kidney and increased accumulation of haemosiderin in the spleen.	
Relevant NOAEL ‡	200 mg/kg bw/day in rats 19.9 mg/kg bw/day 12-month oral study in dog	
Carcinogenicity ‡	Non-carcinogenic in rats and mice	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Reduction in viability and lactation indices, body weight and the morphological development was impaired in the offspring.	
Relevant parental NOAEL ‡	3000 ppm (approximately 320 mg/kg b.w./day).	
Relevant reproductive NOAEL ‡	3000 ppm (approximately 320 mg/kg b.w./day).	
Relevant offspring NOAEL ‡	3000 ppm (approximately 320 mg/kg b.w./day).	

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

Developmental toxicity

Developmental target / critical effect ‡	No evidence of developmental effects at the highest maternally toxic test dose levels in rats and rabbits.	
Relevant maternal NOAEL ‡	150 mg/kg bw/day in rats based on clear effect on food consumption, body weight, clinical symptoms (reversible) during treatment period at 300 mg ai/kg bw/day 50 mg/kg bw/day in rabbits based on decreased food consumption and body weight loss.	
Relevant developmental NOAEL ‡	300 mg/kg bw/day in rats and 150 mg/kg bw/day in rabbits the highest test dose levels in the respective studies.	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	100 mg/kg bw (58 mg as/kg bw). based on signs of toxicity in the qualitative functional observation battery of tests and motor activity tests based on observations of decreased motor activity at 300 mg as/kg bw. The clinical effects observed were explained by reactivity with nicotinergic and muscarinergic receptors and represents a reversible binding to receptors rather than irreversible neurotoxicity.	
Repeated neurotoxicity ‡	13000 ppm (517 mg/kg bw/day in males and 617 mg/kg bw/day in females) based on the absence of neurotoxicity at the highest test dose.	
Delayed neurotoxicity ‡	No structural similarity with substances known to cause delayed neurotoxicity.	
Developmental neurotoxicity	NOAEL in pups 30 mg mepiquat/kg bw/day (no neurotoxic effects but high mortality in pups from 60 mg mepiquat/kg bw/ day on))	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	

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

Studies performed on metabolites or impurities ‡	4-hydroxy mepiquat chloride: LD50 of >464 mg/kg bw negative in the *Salmonella typhimurium* and *Escherichia coli* reverse mutation assays using the standard plate and pre-incubation methods.

Medical data ‡ (Annex IIA, point 5.9)

The Notifier states that the manufacturing plant personnel are surveyed by regular medical examinations This surveillance programme is not aimed to specifically detect mepiquat chloride-related symptoms or diseases. Thus, it does not indicate a causal association between the compound and any specific medical effect. However, frequency and distribution of medical diagnoses in the manufacturing plant personnel did not reveal any peculiarities. No case of incidental exposure to mepiquat chloride has been observed at BASF sites. No specific epidemiological studies in the general population have been reported.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.2 mg/kg bw/day	12-month dietary study in dogs	100
AOEL ‡	0.3 mg/kg bw/day	3 month dietary study in dogs	100
ARfD ‡	0.3 mg/kg bw/day	Developmental neurotoxicity study in rats	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (Terpal)	Based on an in vivo study in rats, 3% for concentrate and diluted

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Total systemic exposures 10% and 70% of the AOEL with the German model and the UK POEM, respectively).
Workers	Exposure estimates 3.5% of the AOEL
Bystanders	Exposure estimates <1% of the AOEL

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

RMS/peer review proposal

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

Substance classified	For the active substance: Hazard symbol: Xn. Indication of danger: Harmful. Risk phrases: R20/22 Harmful by inhalation and if swallowed Safety phrases: S2 Keep out of the reach of children S13 Keep away from food, drink and animal feedingstuffs. S46 If swallowed, seek medical advice immediately and show this container or label S51 Use only in well-ventilated areas For the preparation Hazard symbol: Xn Indication of danger: Harmful Risk phrases: R22 Harmful if swallowed Safety phrases: S2 Keep out of the reach of children S13 Keep away from food, drink and animal feedingstuffs. S23 Do not breathe spray S46 If swallowed, seek medical advice immediately and show this container or label

‡ End point identified by the 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	Cereals (Wheat, Barley), Oilseeds (Cotton) and Fruit (Grape)
Rotational crops	Lettuce, Wheat and Radish
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Wheat and barley
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	Sum of mepiquat and its salts, expressed as mepiquat chloride
Plant residue definition for risk assessment	Sum of mepiquat and its salts, expressed as mepiquat chloride
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	Goat and hens
Time needed to reach a plateau concentration in milk and eggs	Milk – 3 days Eggs – no plateau was reached after 6 days. However the animal transfer study indicated that a plateau was reached after 10 days.
Animal residue definition for monitoring	Sum of mepiquat and its salts, expressed as mepiquat chloride
Animal residue definition for risk assessment	Sum of mepiquat, 4-hydroxy mepiquat and their salts, expressed as mepiquat chloride
Conversion factor (monitoring to risk assessment)	open (data gap)
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

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

	Rotational crop metabolism study indicates that a 'cold' rotational crop study is not required.

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

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

Freezer storage stability study indicated that residues of mepiquat chloride in wheat, wheat products (up to 12 months) and animal products are stable for up to 24 months.

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes *provisional estimates:* [#] 3.1 (dairy cattle) 6.7 (beef cattle	Yes *provisional estimate:*[#] 1.3 (chicken)	Yes *provisional estimate:* [#] 1.5
Potential for accumulation (yes/no):	Yes	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Yes	No	No
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) cattle: 13 mg/kg diet (0.4 mg/kg bw) poultry: 1 and 5 mg/kg diet (0.09 and 0.44 mg/kg bw) Residue levels in matrices : Mean (max) mg/kg *provisional estimates:* [3], [4]		
Muscle	0.05	0.05	0.05
Liver	0.1	0.05	0.05
Kidney	0.1	0.05	0.05
Fat	0.05	0.05	0.05
Milk	0.05		
Eggs		0.05	

[#] based on barley only. Estimation of livestock exposure to be finalised upon completion of the residue trial data base for cereals and under consideration of relevant processing factors for cereals other than barley (i.e. wheat and rye bran)

[3] Residues of mepiquat-chloride only; the 4-hydroxy mepiquat metabolite was not determined in the feeding studies (data gap for a conversion factor)

[4] . Estimated residues in food of animal origin to be reconsidered when livestock dietary burden was recalculated, and when outstanding information to assess residue levels of 4-hydroxy mepiquat in animal matrices is available

‡ End point identified by the 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)
Barley	N	Grain: 0.09, 0.39, 0.45, 0.53, 0.55, 0.73, 0.75, 1.0, 1.5 mg/kg Straw: 1.1, 1.2, 2.1, 2.3, 2.3, 2.4, 2.5, 4.6, 5.9 mg/kg	No trials available to support the cGAP for cereals other than barley	2 mg/kg	Grain: 1.5 Straw: 5.9	Grain: 0.55 Straw: 2.3

(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

‡ End point identified by the 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)

Note: Consumer risk assessment ***not finalised*** for notified representative use

ADI	0.2
TMDI (% ADI) according to WHO European diet	<6% ADI (when barley only is considered)[5]
TMDI (% ADI) according to national (to be specified) diets	Not applicable
IEDI (WHO European Diet) (% ADI)	Not applicable
NEDI (specify diet) (% ADI)	The total NEDIs for UK adults, children, toddlers, infants, vegetarians and the elderly are all less than 3% ADI (when barley only is considered)
Factors included in IEDI and NEDI	No transfer factors were used in calculating the NEDIs
ARfD	0.3
IESTI (% ARfD)	Not applicable
NESTI (% ARfD) according to national (to be specified) large portion consumption data	The NESTIs for UK adults, children, toddlers, infants, vegetarians and the elderly are all 3% or less of the ARfD. [6]
Factors included in IESTI and NESTI	None specified

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	
Pearl barley	4	0.7	n/a	-
Beer	4	0.2	n/a	-
Bran	4	3	n/a	-
Flour	4	0.2	n/a	-
Wholemeal flour	4	0.9	n/a	-
Wholemeal bread	4	0.6	n/a	-

[5] Chronic intake estimates not peer reviewed; submitted by RMS in revised addendum 7 and in comments on EFSA draft conclusion after the meeting of experts
[6] Acute intake estimates not peer reviewed; submitted by RMS in revised addendum 7 and in comments on EFSA draft conclusion after the meeting of experts

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

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

Cereals	Unable to conclude due to lack of data
Food of animal origin	Unable to conclude due to lack of data

Note: If deviating from the notified representative use on cereals a use of mepiquat-chloride on **barley only** were considered, the following MRL proposals could be applicable[7]:

Barley grain	2 mg/kg
Milk, Meat, Fat, Egg	0.05 mg/kg
Kidney, Liver	0.1 mg/kg

[7] Modification of notified representative use and resulting MRL proposals were not considered by the meeting of experts

‡ End point identified by the 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 ‡	43.1-69.7% after 120 d at 20°C, [^{14}C-2,6]-label (n= 4) 17.8% after 120 d at 10°C, [^{14}C-2,6]-label (n= 1)
Non-extractable residues after 100 days ‡	15.8-43.7% after 120-121 d at 20°C, [^{14}C-2,6]-label (n= 4) 31.3% after 120 d at 10°C, [^{14}C-2,6]-label (n= 1)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	None detected at >10% AR, [2,6-^{14}C]-label

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

Anaerobic degradation ‡

Mineralization after 100 days	Mineralisation - no significant mineralisation after 60 d (n = 1)
Non-extractable residues after 100 days	Non-extractable residues – no significant increase in unextracted residues after 60 d (n = 1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None detected at >10% AR, [2,6-^{14}C]-label

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None detected at >10% AR, [2,6-^{14}C]-label (n=1)

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

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

Laboratory studies ‡

Parent	Aerobic conditions					
Soil type	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Neuhofen, loamy sand	6.8*	20 / 40MWHC	31 / 102	23	0.92	SFO, non-linear regression
Holly Springs, loamy sand	5.7	25 / 75% FC at 1/3 Bar	6 / 18	5	0.96	SFO, non-linear regression
Bruch West, sandy loam	7.5	20 / 40	40 / 133	37	0.97	SFO, non-linear regression
Li35b, sandy loam	7.0	20 / 40	11 / 37	8	0.98	SFO, non-linear regression
Lufa 2.2, loamy sand	5.8	20 / 40	11 / 36	11	0.97	SFO, non-linear regression
Meckenheim, loamy sand	6.8*	20 / 40	20 / 65	14	0.99	SFO, non-linear regression
Bruch West, loamy sand	7.5	10 / 40	83 / 277	-	0.95	SFO, non-linear regression
Arithmetic mean / geometric mean				16 / 13.2		

* determined in $CaCl_2$.

Field studies ‡

No data submitted – none required

pH dependence ‡	No
Soil accumulation and plateau concentration ‡	No data submitted – none required.

Laboratory studies ‡

Parent	Anaerobic conditions: No significant degradation

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH (H_2O)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Greenville, loam	0.6	6.3	-	-	9.88	1563	0.958
Woodland, clay	1.1	6.6	-	-	12.00	1099	0.991
Dinuba, sand loam	0.5	6.8	-	-	25.00	4833	0.946
Hokkaido Tokachi, clay loam	2.6	6.2	-	-	1.71	67	0.972
Aichi, Japan, sandy clay loam	0.8	7.1	-	-	5.49	722	0.953
Miyazaki, Japan, sand	1.5	7.2	-	-	1.69	113	0.988
Pfungstadt (22°C)	0.6	7.3*	-	-	13.36	2304	0.972
Pfungstadt (18°C)	0.6	7.3*	-	-	17.06	2942	0.980
Neuhofen (22°C)	2.7	6.1*	-	-	5.74	216	0.963
Neuhofen (18°C)	2.7	6.1*	-	-	7.41	278	0.933
Lufa 2.1 (22°C)	0.5	6.8*	-	-	3.90	765	0.976
Lufa 2.1 (18°C)	0.5	6.8*	-	-	5.17	1014	0.914
median						890	0.968
pH dependence	No For FOCUS gw modelling – K_f: parent, site specific K_f and $^1/_n$ values selected, since no dependence of sorption on organic carbon content (see FOCUS groundwater section for further details of parameters selected)						

*pH determined in KCl

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

Column leaching ‡	No data submitted – none required
Aged residues leaching ‡	Guideline: BBA IV: 4-2, 1996 and SETAC 1995 Aged for (d): 30 d Time period (d): 2 d Precipitation (mm): 200 mm Leachate: 0.1% total radioactivity in leachate All radioactivity present as active substance >60% total radioactivity retained in top 24 cm
Lysimeter/ field leaching studies ‡	No data submitted – none required

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

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	DT_{50} (d): 40 days Kinetics: 1st order Field or Lab: longest DT_{50} from laboratory studies.
Application data	Crop: wheat % plant interception: 70% for elongation stage Number of applications: 1 Application rate(s): 762.5 g as/ha

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.305		-	
Short term	24h	0.300	0.302	-	-
	2d	0.295	0.300	-	-
	4d	0.285	0.295	-	-
Long term	7d	0.270	0.287	-	-
	28d	0.188	0.242	-	-
	50d	0.128	0.204	-	-
	100d	0.054	0.145	-	-

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

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 3, 5, 7 and 9: 25°C, hydrolytically stable
Photolytic degradation of active substance and metabolites above 10 % ‡	Artificial light, photolytically stable
Quantum yield of direct phototransformation in water at Σ > 290 nm	Not determined – photolytically stable
Readily biodegradable ‡ (yes/no)	Yes. Under the conditions of the test (OECD No. 301A), DOC die away reached a maximum of 100% of the theoretical over the course of the 35 d incubation with an activated sludge inoculum (degradation occurred within a 10 d window). An adsorption control was run for 5 d and indicated that mepiquat chloride was not eliminated by adsorption over this period. Hence mepiquat chloride is classified as 'readily biodegradable' according to OECD criteria.

Degradation in water / sediment

Parent	Distribution (Max. sed 56.2 % after 14 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Kellmetschweiher, Germany	8.45	5.8	20	32-107	0.99	Nd*		25-83	0.94	SFO, non-linear regression
Ranschgraben, Germany	7.80	4.8	20	33-109	0.99	Nd*		22-73	0.97	SFO, non-linear regression
Arithmetic mean				32.5				23.5		

*the dissipation DT50 value from the water phase was 6 and 9 days in the two systems respectively.

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

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
Kellmetschweiher Germany	8.45	5.8	65.8% after 100d (end of study)	58.2% after 30 d	25.7% after 100 d (end of study)
Ranschgraben, Germany	7.80	4.8	61.7% after 100 d (end of study)	62.6% after 30 d	26.7% after 100 d (end of study)

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

Parent (mepiquat chloride) Parameters used in FOCUSsw step 1 and 2	1st order DT_{50} soil (STEP 1 and 2): 20 days (mean from laboratory aerobic soil degradation studies, without normalisation, n = 6) 1st order DT_{50} whole system (STEP 1): 33 days (worst case from two systems) 1st order DT_{50} water (STEP 2): 999 days (no degradation in water assumed as worst case) 1st order DT_{50} sediment (STEP 2): 25 days (worst case from two systems) Mepiquat chloride molecular weight = 149.7 K_{OC}: 890 l/kg median from soil adsorption studies (n = 12)
Parameters used in FOCUSsw step 3 (if performed)	Not required since acceptable risk assessment using Step 1 and 2 PEC values. RMS confirmed that Step 3 gave lower PECsw values than Step 2.
Application rate	Crop: wheat Number of applications: 1 % plant interception: average crop cover assumed, therefore 50% interception assumed at STEP 2 only – no interception assumed at STEP 1. Application rate(s): 762.5 g as/ha Depth of water body: 30 cm

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

Main routes of entry

Parameter	STEP 1	STEP 2	
		Europe, North	Europe, South
Distance to the water body (m):	1.00	1.00	1.00
Spraydrift (% of application):	2.759	2.759	2.759
Runoff + drainage (% of application):	10	2	4
Ratio of field to water body:	10	10	10

FOCUS$_{SW}$ STEP 1

PEC$_{(sw)}$ (µg / l)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	123.2		-	-
Short term 24h	117.0	120.1	-	-
2d	114.5	117.9		
4d	109.8	115.0		
Long term 7d	103.1	111.3	-	-
14d	89.0	103.6		
21d	76.8	96.7		
28d	66.3	90.4		
42d	49.4	79.4		
50d	41.8	74.0		
100d	14.6	49.9		

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

$FOCUS_{SW}$ STEP 2

$PEC_{(sw)}$ (µg/l) Time after maximum peak[8]	Europe, North		Europe, South	
	Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Initial	13.9	-	24.0	-
Short term 24h	13.2	13.5	23.3	23.7
2d	13.0	13.3	22.9	23.4
4d	12.6	13.0	22.2	23.0
Long term 7d	12.0	12.7	21.2	22.4
14d	10.8	12.1	19.1	21.3
21d	9.7	11.5	17.2	20.2
28d	8.7	10.9	15.4	19.2
42d	7.0	9.9	12.4	17.5
50d	6.2	9.4	11.0	16.5
100d	2.9	6.9	5.1	12.1

$FOCUS_{SW}$ PEC (sediment)

Parent

Method of calculation and application rate	As per $FOCUS_{SW}$ above

$FOCUS_{SW}$ STEP 1

$PEC_{(sed)}$ (µg/kg dry sediment)	Single application Actual	Single application Time weighted average
Initial	1.03E+03	-
Short term 24h	1.04E+03	1.04E+03
2d	1.02E+03	1.03E+03
4d	977.4	1.02E+03
Long term 7d	917.7	986.5
14d	792.2	920.0
21d	683.9	858.9
28d	590.4	803.2
42d	440.0	705.9
50d	371.9	657.8
100d	130.1	444.0

[8] Maximum peak PEC_{SW} occurred on day 4 following application in STEP 2 calculation

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

FOCUS$_{SW}$ STEP 2

PEC$_{(sed)}$ (µg/kg dry sediment) Time after maximum peak[9]	Europe, North		Europe, South	
	Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
Initial	114.1	-	201.8	-
Short term 24h	112.3	113.2	201.7	201.8
2d	110.6	112.3	198.6	200.9
4d	107.3	110.7	192.6	198.3
Long term 7d	102.5	108.2	184.0	194.0
14d	92.1	107.7	165.3	184.3
21d	82.8	97.6	148.6	175.1
28d	74.4	92.8	133.5	166.6
42d	60.1	84.2	107.8	151.1
50d	53.2	79.8	95.4	143.2
100d	24.8	58.5	44.5	104.9

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUS gw scenarios, according to FOCUS guidance. Model(s) used: FOCUS PELMO (v 3.3.2) Scenarios (list of names): Châteaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Seville, Thiva Crop: Winter wheat Mepiquat chloride molecular weight = 149.7 Arithmetic mean parent DT_{50lab} 16 d (normalisation to 10kPa or pF2, 20°C with Q10 of 2.2). K_f: parent, site specific K_f and $^1/_n$ values selected, since no dependence of sorption on organic carbon content shown:-
Application rate	Application rate: 762.5 g/ha. No. of applications: 1 Interception: 70% Time of application (month or season): spring

[9] Maximum peak PEC_{Sed} occurred on day 5 following application in STEP 2 calculation

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

PEC(gw) - FOCUS scenario specific input values for adsorption

Scenario Horizon #	Châteaudun	Hamburg	Jokioinen	Kremsmünster	Okehampton	Porto	Piacenza	Seville	Thiva
Kf									
1	12.0	1.69	5.74	9.88	1.71	5.741	9.88	9.88	9.88
2	12.0	1.69	3.9	9.88	9.88	5.741	9.88	9.88	9.88
3	9.88	3.9	3.9	25	25.0	5.741	3.9	9.88	9.88
4	25	0	3.9	25	25.0	5.741	3.9	9.88	25.0
5	25	0	3.9	25	25.0	-	0	9.88	25.0
6	25	0	3.9	-	-	-	0	9.88	25.0
7	25	-	-	-	-	-	-	-	-
1/n									
1	0.991	0.988	0.963	0.958	0.972	0.963	0.958	0.958	0.958
2	0.991	0.988	0.976	0.958	0.958	0.963	0.958	0.958	0.958
3	0.958	0.976	0.976	0.946	0.946	0.963	0.976	0.958	0.958
4	0.946	---	0.976	0.946	0.946	0.963	0.976	0.958	0.946
5	0.946	---	0.976	0.946	0.946	-	---	0.958	0.946
6	0.946	---	0.976	-	-	-	---	0.958	0.946
7	0.946	-	-	-	-	-	-	-	-

Maximum concentration	Not applicable
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 for all scenarios. In addition the Rapporteur repeated modelling with a median Koc of 890 and 1/n value of 1.0, and all PECgw values were also <0.001µg/l for all scenarios.

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

Direct photolysis in air ‡	No data submitted - none required
Quantum yield of direct phototransformation	No data submitted - none required
Photochemical oxidative degradation in air ‡	DT_{50} of 4.56 hours on the basis of the assumption of 1.5 x 10^6 OH radicals/cm^3. This equates to 0.38 days assuming a 12 hr light day (derived by the Atkinson method of calculation)
Volatilisation ‡	No data submitted

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

PEC (air)

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	Negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: mepiquat chloride Surface Water: mepiquat chloride Sediment: mepiquat chloride Ground water: mepiquat chloride Air: mepiquat chloride

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

Soil (indicate location and type of study)	No data submitted
Surface water (indicate location and type of study)	No data submitted
Ground water (indicate location and type of study)	No data submitted
Air (indicate location and type of study)	No data submitted

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

None applicable

‡ End point identified by the 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)

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Colinus virginianus	a.s.	Acute	LD50 > 2000	NR
	Preparation	Acute	NA	NA
Colinus virginianus	a.s.	Short-term	LD50> 1326	LC50=>5637
Coturnix coturnix Japonica	a.s.	Long-term	NOED 100.7	NOEC=933
Mammals ‡				
rat	a.s.	Acute	LD50 200	NR
	Preparation	Acute	NR	NR
rat	a.s.	Long-term	NOAED 155	NR
Additional higher tier studies ‡ None submitted or required.				

NR = not relevant NA= not available.

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

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

Winter wheat and winter and spring barley. One application/crop at 762.5 g mepiquat chloride/ha between BBCH growth stages 31-49

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivore Late	Acute	41.24	> 48.50	10
Insectivore Late	Short-term	23.00	> 57.65	10
Insectivore Late	Long-term	23.00	4.4	5
Higher tier refinement (Birds): Refinement of acute and dietary risk not required. Refinement of long term risk using NOED 100.7 mg/Kg bw, PT = 0.99, PD = 0.23 small seeds, 0.385 small insects and 0.385 large insects results in a TER =8.53				
Tier 1 (Mammals)				
Insectivore Late	Acute	6.73	29.7	10
Insectivore Late	Long-term	2.45	63.3	5
Higher tier refinement (Mammals): Not required				

‡ Endpoints identified by 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 (Test type)	End point	Toxicity (mg/L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss	a.s.	96 hr (static)	Mortality, LC_{50}	>100 mg mepiquat chloride/L n
Oncorhynchus mykiss	a.s.	28 d (flow through)	Growth NOEC	100 mg mepiquat chloride/L n
Oncorhynchus mykiss	a.s.	95 d early life stage (flow-through)	Development NOEC	100 mg mepiquat chloride/L n
Oncorhynchus mykiss	'BAS 098 00W'	96 hr (static)	Mortality, LC_{50}	>100 mg formulation/L n
Aquatic invertebrate				
Daphnia magna	a.s.	48 h (static)	Mortality, EC_{50}	68.5 mg mepiquat chloride/L n
	a.s.	21 d (semi-static)	Reproduction, NOEC	12.5 mg mepiquat chloride/L n

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg/L)
Daphnia magna	'BAS 098 00W'	48 h (static)	Mortality, EC_{50}	>100 mg formulation/L n
Daphnia magna	a.s.	21 d (static renewal)	Reproduction, NOEC	12.5 mg mepiquat chloride/L n
Sediment dwelling organisms				
Study not submitted or required.				
Algae				
Anabaena flos-aquae.	a.s.	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	14.4 44.8 mg mepiquat chloride/L n
Pseudokirchneriella subcapitata	'BAS 098 00W'	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	>1000 >1000 mg formulation/L n
Higher plant				
Lemna gibba	a.s.	14 d (static)	Fronds, EC_{50} E_bC50 E_rC50	 2.6 15.41 mg mepiquat chloride/L n

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg/L)
	'BAS 098 00W'	14 d (static)	E_bC50 E_rC50 Fronds, EC_{50}	16.507 >100 mg formulation/L n
Microcosm or mesocosm tests: Not required				

n = nominal concentration
'BAS 098 00W' contains nominally 305 g mepiquat chloride and 155 g ethephon/L

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

FOCUS Step1

Winter wheat and winter and spring barley. One application/crop at 762.5 g mepiquat chloride/ha between BBCH growth stages 31-49

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	Annex VI Trigger
a.s.	Fish	>100	Acute	0.1232	NR	>8117	100
a.s.	Fish	100	Chronic	0.1232	NR	811.7	10
a.s.	Aquatic invertebrates	68.5	Acute	0.1232	NR	556	100
a.s.	Aquatic invertebrates	12.5	Chronic	0.1232	NR	101.5	10
a.s.	Algae	14.4	Chronic	0.1232	NR	116.9	10
a.s.	Higher plants[2]	2.6	Chronic	0.1232	NR	21.1	10

NR = not relevant

Since the Annex VI of 91/414EEC triggers were met for all groups of organisms at FOCUS Step 1 there was no need to calculate TERs at subsequent Steps.

Bioconcentration: No study submitted and none required as log P_{ow} < 3

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)
Mepiquat chloride	> 107.4 mepiquat chloride	> 100 mepiquat chloride

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

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
'BAS 098 00W'	> 247.1 'BAS 098 00W'	> 214.1 'BAS 098 00W'
Field or semi-field tests: Not required		

'BAS 098 00W' contains nominally 305 g mepiquat chloride and 155 g ethephon/L

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

Winter wheat, winter and spring barley. One application/crop at 762.5 mg mepiquat chloride/ha between BBCH growth stages 31-49.

Test substance	Route	Hazard quotient	Annex VI Trigger
Mepiquat chloride	Oral	< 7.1	50
Mepiquat chloride	Contact	< 7.6	50
Preparation: 'BAS 098 00W'	Oral	< 11.1	50
Preparation: 'BAS 098 00W'	Contact	< 12.6	50

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ‡	'BAS 083 52 W' (617.6 g mepiquat chloride/L)	Mortality	1530 g mepiquat chloride/ha
Aphidius rhopalosiphi ‡	'BAS 083 52 W' (617.6 g mepiquat chloride/L)	Mortality	1366 g mepiquat chloride/ha
Typhlodromus pyri ‡	'BAS 098 00W' (308.2 g mepiquat chloride/L and 158.9 g ethephon/L)	Mortality	3360 mL product/ha

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

Winter wheat, winter and spring barley. One application/crop at 762.5 g mepiquat chloride/ha between BBCH growth stages 31-49

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
'BAS 083 52 W' (617.6 g mepiquat chloride/L)	*Typhlodromus pyri*	1530 g mepiquat chloride/ha	< 0.5	-	2
'BAS 083 52 W' (617.6 g mepiquat chloride/L)	*Aphidius rhopalosiphi*	1366 g mepiquat chloride/ha	< 0.56	-	2
'BAS 098 00W'	*Typhlodromus pyri*	3360 mL 'BAS 098 00W'/ha	0.79	-	2

[1] Since the in-field HQs are< 2 the off-field HQs will be no higher and there is no need for detailed calculations

Since the HQs for the standard sensitive species are <2 the risk is acceptable and there is no requirement for further data for the use currently proposed. However extended laboratory studies and studies on other species have been submitted and the endpoints are summarized here for future reference.

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (mL product/ ha) initial residues	End point	% effect (+ indicates adverse effect. - indicates positive effect.)	Trigger value
Typhlodromus pyri	Proton ymphs < 1 day old	'BAS 098 00W' bean leaf 14 days (7 mortality + 7 reproduction)	90 450 3000	Mortality (% corrected)	1.2 1.2 19.8	50 %
			0 90 450 3000	Reproduction (eggs/female)	6.4 6.6 7.4 6.3	

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

Species	Life stage	Test substance, substrate and duration	Dose (mL product/ ha) initial residues	End point	% effect (+ indicates adverse effect. - indicates positive effect.)	Trigger value
Aphidius rhopalosiphi	Adults 2 days old	'BAS 098 00W' barley seedlings 48 h	90 450 3000 0 90 450 3000	Mortality (% corrected) Reproduction (mummies/female)	3.3 0 0 30.6 31.9 33.7 26.9	50 %
Chrysoperla carnea	Larvae 2-3 days old	'BAS 098 00W' glass	375 750 1500 2500 5000 0 375 750 1500 2500 5000	Mortality (% corrected) Reproduction (eggs/female)	0 9 4 22 6 23.5 23.6 23.1 19.1 26.2 24.6	50 %
Aleochara billineata	Adults 2-6 days old	'BAS 098 00W' Sand	0 3000	Reproduction. No. beetles emerging from pupation	818.5 823	50 %

Field or semi-field tests: Not required

‡ Endpoints identified by 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)

Test organism	Test substance	Time scale	End point[1]
Earthworms			
Eisenia foetida	Mepiquat chloride	Acute 14 days	LC_{50} 319.5 mg a.s./kg d.w.soil
Eisenia foetida	Mepiquat chloride	Chronic 8 weeks	No study submitted or required
	'BAS 098 00W'	Acute	LC_{50} 299 mg formulation/kg d.w.soil
	Preparation	Chronic	No study submitted or required
	Metabolite	Acute	No study submitted or required
	Metabolite	Chronic	No study submitted or required
Other soil macro-organisms			
Soil mite	No studies submitted or required		
Collembola	No studies submitted or required		
Soil micro-organisms			
Nitrogen mineralisation	'BAS 083 34W' (50 g mepiquat chloride/L)	28 days	< 25% effect at day 28 at 1.352 mg mepiquat chloride/kg d.w.soil (20L product/ha)
Carbon mineralisation	'BAS 083 34W' (50 g mepiquat chloride/L)	84 days	< 25% effect at day 84 at 1.352 mg mepiquat chloride/kg d.w.soil (20L product/ha)
Nitrogen mineralisation	'BAS 098 00W' [2] (305 g mepiquat chloride and 155 g ethephon/L)	28 days	< 25% effect at day 28 at 8.14 mg mepiquat chloride/kg d.w.soil (20L product/ha)
Carbon mineralisation	'BAS 098 00W' [2] (305 g mepiquat chloride and 155 g ethephon/L)	28 days	< 25% effect at day 28 at 8.14 mg mepiquat chloride/kg d.w.soil (20L product/ha)
Field studies: None submitted or required.			

[1] No correction required as log P_{ow} < 2.
[2] The worst case assumption that all the toxicity is attributable to mepiquat chloride has been made.

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

Toxicity/exposure ratios for soil organisms

Winter wheat, winter and spring barley. One application/crop at 762.5 mg mepiquat chloride/ha between BBCH growth stages 31-49.

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
Eisenia foetida	'BAS 083 52W' (50 g mepiquat chloride/L)	Acute	0.305 mg mepiquat chloride/kg soil	1048	10
Eisenia foetida	'BAS 098 00W' (50 g mepiquat chloride/L)	Acute	1.092 mg formulation/kg	274	10

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

Not submitted and not required.

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha)[2] vegetative vigour mL formulation/ha	ER_{50} (g/ha) emergence mL formulation/ha	Exposure[1] mL formulation/ha	TER	Trigger
Daucus carota	'BAS 098 00W' (308.2 g mepiquat chloride and 158.8 g ethephon/L)	> 3000	>3000	69.25	43.32	5
Linum usitatissimum		> 3000	> 3000	69.25	43.32	5
Brassica napus		> 3000	>3000	69.25	43.32	5
Pisum sativum		> 3000	> 3000	69.25	43.32	5
Avena sativa		> 3000	> 3000	69.25	43.32	5
Allium cepa		> 3000	> 3000	69.25	43.32	5

[1] Based on Ganzelmeier drift data at 3m, 2.77% of applied spray

Additional studies (e.g. semi-field or field studies)

None submitted or required.

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

Test type/organism	End point
Activated sludge respiration	> 1000 g mepiquat chloride/L

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

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

Compartment	
soil	Parent (mepiquat chloride)
water	Parent (mepiquat chloride)
sediment	Parent (mepiquat chloride)
groundwater	Parent (mepiquat chloride)

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

	RMS/peer review proposal
Active substance	R51 Toxic to aquatic organisms R53 May cause long term adverse effects in the aquatic environment. N Dangerous for the environment S60 This material and its container must be disposed of as hazardous waste. S61 Avoid release to the environment. Refer to special instructions/Safety Data Sheet.
Preparation 'BAS 098 00W'	R52 Harmful to aquatic organisms R53 May cause long term adverse effects in the aquatic environment. Dangerous for the environment S35 This material and its container must be disposed of in a safe way. S 57 Use appropriate containment to avoid environmental contamination.

‡ Endpoints identified by 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
ER50	emergence rate, median
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
NOEC	no observed effect concentration
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
-	-	-
-	-	-
-	-	-