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

formetanate

finalised: 24 April 2006

SUMMARY

Formetanate is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[1], as amended by Commission Regulation (EC) No 1490/2002[2]. This Regulation requires the European Food Safety Authority (EFSA) to organise 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 one year a conclusion on the risk assessment to the EU-Commission.

Italy being the designated rapporteur Member State submitted the DAR on formetanate in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 13 July 2004. Following a quality check on the DAR, the peer review was initiated on 23 July 2004 by dispatching the DAR for consultation of the Member States and the sole applicant Margarita Internacional. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting on 9 February 2005. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in June and July 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 6 April 2006 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as acaricide and insecticide comprise broadcast spraying to control the thrips and mites in tomatoes and ornamental shrubs at an application rate of 500 g formetanate per hectare. Formetanate can be as acaricide and insecticide.
The representative formulated product for the evaluation was "Dicarzol 500 SG" ("AEB036056 00 SG58 A200"), a water soluble granule (SG), registered in France, Portugal and Spain.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. formetanate and its salts in food of plant origin, soil and water.

[1] OJ No L 53, 29.02.2000, p. 25
[2] OJ No L 224, 21.08.2002, p. 25

In the case of air it should be noted that the analytical method is not specific as required in, because it is not possible to differentiate between residue of formetanate and its salts.
Also an analytical method for blood (plasma) is available to cover Annex point 4.2.5 of Directive 96/46/EC.
Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Formetanate hydrochloride is rapidly and extensively absorbed after oral administration. It is mainly excreted in urine. No tendency for bioaccumulation was observed.
It is highly toxic after oral administration and by inhalation, not toxic after dermal exposure, not irritant, but a skin sensitizer. The proposed classification is: T^+, R26/28 “Highly toxic by inhalation and if swallowed”; Xi, R43 “May cause sensitisation by skin contact”.
Short term toxicity is manifested by cholinesterase inhibition in all species, the dog being the most sensitive. Formetanate hydrochloride has a mutagenic potential in vitro, but not in vivo, and there is no evidence of carcinogenicity in rats and mice. No reproductive or teratogenic effects have been observed in rats and rabbits. All the tested metabolites are less toxic than formetanate hydrochloride. The kinetics of cholinesterase inhibition was studied in female rats and in dogs.
The Acceptable Daily Intake (ADI) is 0.004 mg/kg bw/day, the Acceptable Operator Exposure Level (AOEL) is 0.004 mg/kg bw/day, and the Acute Reference Dose (ARfD) is 0.005 mg/kg bw. All the reference values were derived with a safety factor of 100.
According to the German model, the estimated operator exposure during field use is 55% of the AOEL with PPE for the tractor mounted scenario, and 99% of the AOEL with PPE and RPE for the hand held scenario. According to calculations with the German and UK models, application with automated gantry sprayers in glasshouse gives an operator exposure of 31 and 8.3% of the systemic AOEL with PPE. The worker exposure (during tomatoes harvest) and the bystander exposure estimates are below the AOEL.

The metabolism of formetanate in plants has been fully elucidated and proceeds through hydrolysis steps. The parent compound has been identified as the major constituent of the residue on various crops and for various PHIs. The identified metabolites are less toxic than the parent compound. Therefore the residue definition can be restricted to parent compound only, for both risk assessment and monitoring. Under processing, formetanate is degraded at temperature of 100°C or higher to a less toxic compound, 3-hydroxyformanilide. The processed commodities obtained after boiling or sterilisation have a significantly lower concentration of formetanate than raw tomatoes.
There is no exposure of livestock to formetanate residues. The soil uptake by rotational crops is minimal and there is no need for setting plant back restriction.
The chronic exposure of the consumer is well below the ADI of formetanate.

Acute intake calculations have indicated a potential acute risk for infants and toddlers resulting from the consumption of treated tomatoes grown under glass house conditions. The level of the proposed MRL in tomatoes, which is significantly higher than the level considered in exposure assessments, causes still higher concern in terms of consumer safety.

In acidic soils the main sink for the dissipation of formetanate was the formation of unextracted residues with mineralisation to CO_2 accounting for 2.7-13.7% of the applied radioactivity (AR) at 41 to 91 days. However in an alkaline soil (pH 7.2), after 59 days mineralisation to CO_2 accounted for 80%AR with unextracted residue accounting for only 9.2%AR. No major (>10%AR) breakdown products were identified in methanol or water extracts. The use of a more harsh methanol Soxhlet extraction released more radioactivity from soil samples, but was also shown to hydrolyse formetanate to the major breakdown products 3-FAPMC[3], 3-APMC[4] and 3-HF[5]. As it is not possible to know if the radioactive residue in soil released by methanol Soxhlet extraction was present as parent formetanate or breakdown products, the available environmental exposure assessments have been carried out assuming all the Soxhlet extractable radioactivity was parent formetanate and also, as a worst case assuming 100% conversion of applied formetanate to the breakdown products identified in extracts, which were 3-FAPMC (max 20.2%AR), 3-APMC (max 50.6%AR), 3-HF (max 17.6%AR), 3-HPDMF[6] (max 23%AR in a photolysis study, utilising oven dried soil), and 3-AP[7] (max 5.7%AR). Formetanate exhibits low to moderate persistence in soil. 3-FAPMC exhibits very low persistence, 3-AMPC and 3-HF very low to low persistence with 3-HPDMF exhibiting low persistence in soil.

Formetanate exhibits high to low soil mobility and as it is a basic substance with a pKa of 8.1 would be expected to be more mobile under high soil pH conditions. However the higher mobility under alkali conditions is unlikely to lead to an increased risk of formetanate leaching due to the more rapid hydrolytic degradation of formetanate under alkali soil conditions. There was no evidence that the adsorption of any of the soil metabolites was pH dependant. 3-AMPC exhibits very high to high mobility, 3-FAPMC exhibits high mobility, 3-HF exhibits medium mobility and 3-HPDMF exhibits medium to low mobility in soil. Based on the evidence from FOCUS groundwater scenario modelling for the notified intended uses, the potential for groundwater exposure by formetanate or its potential soil metabolites 3-FAPMC, 3-HPDMF, 3-HF and 3-APMC above the parametric drinking water limit of 0.1µg/L, is considered low.

In natural sediment water systems (laboratory) 20°C formetanate dissipated rapidly from water from a combination of adsorption to sediment and rapid degradation, with formetanate exhibiting very low persistence in both water and sediment. Mineralisation to CO_2 accounted for 14-30%AR after 28-70 days, with unextracted sediment residues being the major sink in the material balance accounting for

[3] 3-FAPMC: 3-formamidophenyl methylcarbamate
[4] 3-APMC: 3-aminophenyl methylcarbamate
[5] 3-HF: 3-hydroxyformanilide
[6] 3-HPDMF: N-(3-hydroxyphenyl)-NN-dimethylformamidine
[7] 3-AP: 3-aminophenol

53-58%AR after 28 days. No major metabolites were present in sediment extracts. In water the major metabolites were 3-HF (max. 39%AR), 3-FAPMC (max. 34%AR), 3-AP (max. 23%AR), 3-APMC (max. 13%AR) and 3-HPDMF (max. 12%AR). These maximum concentrations all occurred between 0.5 and 7 days. These metabolites exhibited very low to low persistence in the water.

The first tier risk assessment for birds indicates acute and long term risk to birds. Short-term TERs were above the trigger but were based on a LC_{50} value that was questioned by the experts' meeting due to strong food avoidance observed in the study. A refined acute and long-term assessment is available based on measured residues in food items and selected focal species. Due to the late submission date this assessment has not been peer reviewed or discussed by Member States. It should be noted that the refined acute assessment is based on the questioned LC_{50} value from a short-term dietary study. Also for mammals the first tier assessment indicated an acute risk, while the long-term risk was considered low. A refined assessment of the acute risk for different focal species taking recommendations given in the PPR Panel opinions for pirimicarb and metamidophos into account is available but has not been peer reviewed. Therefore, no final conclusion on the risk to birds and mammals can be reached at this stage. Formetanate is very toxic to aquatic invertebrates, particularly cladocerans. Based on the results from an available microcosm study the risk is however considered to be low for the evaluated representative uses. Toxicity towards bees and other non-target arthropods is high. Formetanate should not be applied later than two weeks before flowering to protect bees. Even though a potential for in-field recolonisation has been demonstrated, the risk to sensitive non-target arthropods off-field is high even at a distance of 50 m from the field border. Further data is required to fully address the impact off-field and the potential for recolonisation. Furthermore a higher tier study with *T. pyri* is required. The risk to earthworms, other soil macro- and micro-organisms, flora and biological methods of sewage treatment is considered as low.

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

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BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Formetanate is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating Italy as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Italy submitted the report of its initial evaluation of the dossier on formetanate, hereafter referred to as the draft assessment report, to the EFSA on 13 July 2004. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 23 July 2004 to the Member States and the main applicant Margarita Internacional 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, representatives from Member States identified and agreed in an evaluation meeting on 9 February 2005 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier attended this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team of the Pesticide Safety Directorate (PSD) in York, United Kingdom in June and July 2005. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 6 April 2006 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 8(7) of the amended Regulation (EC) No 451/2000, 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 4 March 2005)
- the consultation report

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 7 March 2006)

Given the importance of the draft assessment report including its addendum (compiled version of January 2006 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

Formetanate is the ISO common name for 3-dimethylaminomethyleneiminophenyl methylcarbamate (IUPAC). Due to the fact that the hydrochloride, a variant of formetanate, is used in the formulated product, it should be noted that the evaluated data belong to the variant formetanate hydrochloride, unless otherwise specified.

Formetanate and formetanate hydrochloride, respectively, belong to the class of formamidine acaricide and insecticide such as amitraz and formparanate, respectively. Formetanate acts by contact and ingestion (systemic action) and inhibits the enzyme acetylcholinesterase.

The representative formulated product for the evaluation was "Dicarzol 500 SG" ("AEB036056 00 SG58 A200"), a water soluble granule (SG), registered in France, Portugal and Spain.

The evaluated representative uses as acaricide and insecticide comprise broadcast spraying to control the thrips and mites in tomatoes and ornamental shrubs at an application rate of 500 g formetanate per hectare. Formetanate can be as acaricide and insecticide.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of formetanate as manufactured should not be less than 910 g/kg as formetanate hydrochloride. At the moment no FAO specification exists. The technical material contains no relevant impurities. However, the applicant has to provide data on the identity of one impurity, which has not been identified yet. Moreover, clarification is needed with respect to the proposed specified maximum level for some impurities. Therefore, the specification for the technical material as a whole should be regarded as provisional for the moment.

It became apparent during the peer review process that a new shelf-life study must be provided, due to the fact that in the submitted one only the content of formetanate hydrochloride was determined.
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 formetanate or the respective formulation.

The main data regarding the identity of formetanate and formetanate hydrochloride, respectively and their physical and chemical properties are given in appendix 1.

The content of formetanate in the representative formulation is 500 g/kg (pure) and 582.5 g/kg formetanate hydrochloride (pure), respectively.

Sufficient test methods and data relating to physical, chemical and technical properties are available, being aware that a shelf life study is missing. Also adequate analytical methods are available for the determination of formetanate hydrochloride in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. formetanate and its salts in food of plant origin, soil and water.
In the case of air it should be noted that the analytical method is not specific as required in, because it is not possible to differentiate between residue of formetanate and its salts.
Also an analytical method for blood (plasma) is available to cover Annex point 4.2.5 of Directive 96/46/EC.
The methodology used is HPLC with MS/MS detection. A multi-residue method like the Dutch MM1 or the German S19 is not applicable to due the nature of the residues.
An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.2).

The discussion in the expert meeting (EPCO 30, July 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material, clarification to some physical and chemical properties and the analytical methods with respect to the proposed residue definitions (food and environment). The needed clarification with respect to the partition coefficient and the water solubility is given by the rapporteur Member State in the evaluation table. This information was neither peer reviewed by other Member States nor discussed in the expert meeting.

2. Mammalian toxicology

Formetanate hydrochloride was discussed at the EPCO experts' meeting for mammalian toxicology (EPCO 28) in June and July 2005.

The overall assessment of the toxicological properties is based on the assumption that the batches used are in accordance with the specification of the technical material (reference to Vol. 4, Annex C, C.1.2.3 Analytical profile of batches).

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

Formetanate hydrochloride is rapidly and extensively absorbed after oral administration (>96% within 120 hours). The major route of excretion is urine (> 92 % of the dose), predominantly during the first 24 hours after application (> 70 % of the administered dose). A minor proportion of the administered dose is recovered from faeces (about 4-7% of the dose). No evidence of bioaccumulation is observed. The highest residue levels are found in the liver and gastro-intestinal tract. The metabolism is extensive and involves cleavage, hydroxylation and conjugation.

2.2. Acute toxicity

Formetanate hydrochloride is highly toxic after oral administration (rat LD_{50} 14.8 mg/kg bw, similar results in mice and dogs) and after inhalation (LC_{50} 0.15 mg/L). The acute dermal toxicity is low (LD_{50} > 2000 mg/kg bw). Formetanate hydrochloride is not irritant for the skin and mildly irritating to the eye, but not classified, and a skin sensitizer.

Based on these results, the proposed classification is: **T^+, R26/28 "Highly toxic by inhalation and if swallowed"; Xi, R43 "May cause sensitisation by skin contact"**.

2.3. Short term toxicity

Oral studies were performed with dogs (29-day, 1-year) and rats (90-day). The same effect consisting of acetylcholinesterase (AChE) inhibition is observed in all species. The dog is the most sensitive, with a NOAEL of 0.4 mg/kg bw/day, based on reduced plasma and whole blood AChE activities. The brain AChE was not affected.

The dermal NOAEL after 21 days of exposure in rats is 20 mg/kg bw/day (highest dose tested).

2.4. GENOTOXICITY

The genotoxic properties of formetanate hydrochloride were studied *in vitro*, with test systems using bacterial, yeast and mammalian cells and *in vivo*, with test systems using somatic and germ cells of mice and rats.

Formetanate hydrochloride is positive in a mouse lymphoma assay both with and without activation at highly cytotoxic concentrations. In a chromosome aberration assay *in vitro* using human lymphocytes a clastogenic potential is observed in the absence of metabolic activation. However further testing for the induction of DNA damage and repair *in vitro* leads to negative results.

One *in vivo* mouse bone marrow micronucleus assay, one *in vivo / in vitro* rat liver DNA repair (UDS) test, and one *in vivo* cytogenetic assay using mouse germ cells (spermatogonia) show no mutagenic effect.

Overall, the data indicate that formetanate hydrochloride has a mutagenic potential *in vitro* but not *in vivo.*

2.5. LONG TERM TOXICITY

In the 2-year rat study, based on the inhibition of whole blood, plasma and brain AChE as well as reduced body weights, the NOAEL is 2.3 mg/kg bw/day in males and 2.9 mg/kg bw/day in females.

In the 95-week carcinogenicity study in mice, the NOAEL is 7.0 mg/kg bw/day in males and 9.3 mg/kg bw/day in females, based on reduced body weights in both sexes including an initial body weight loss in females.

Formetanate hydrochloride showed no evidence of carcinogenicity in rats and mice.

2.6. REPRODUCTIVE TOXICITY

The effects of formetanate hydrochloride on the reproductive system have been studied in rats (one and two-generation, and teratogenicity) and in rabbits (teratogenicity).

Reproductive performance and fertility are not affected in the one and two-generation rat studies. Indications of parental toxicity are reduced body weight and AChE inhibition. Offspring toxicity is manifested by reduced body weight gain and viability (F2 litters), at a maternally toxic dose. The NOAELs are:

for parental and offspring toxicity:	4.5 mg/kg bw/day
for the reproductive performance:	22 mg/kg bw/day

In the rat and rabbit teratogenicity studies, the adverse effects observed in dams are reduced body weight gain and food intake as well as cholinergic clinical signs. AChE activity is not measured. No indication of teratogenicity is obtained at any dose level. The rat is more sensitive and the relevant NOAELs are:

for maternal toxicity:	1 mg/kg bw/day
for teratogenicity:	> 5 mg/kg bw/day

2.7. NEUROTOXICITY

The potential of formetanate hydrochloride to induce delayed neurotoxicity was investigated in hens. The results reveal no potential to induce acute delayed neuropathy at a dose level of 23.7 mg/kg bw, i.e. slightly above the acute oral LD_{50} of 21.5 mg/kg bw.

The acute neurotoxicity study by gavage in rats results in a NOAEL of 0.1 mg/kg bw, based on a decrease in brain and whole blood AChE activity.

In a 13-week neurotoxicity study in rats, the NOAEL is 3.0 mg/kg bw/day, based on reduced body weights. There are no effects on behaviour and AChE activities (blood and brain) up to the highest dose tested (18.4 mg/kg bw/day).

2.8. FURTHER STUDIES

Metabolites :

The acute oral toxicity of formetanate hydrochloride and of six metabolites was tested in rats. The metabolites are 3-methylaminomethyleneaminophenyl methyl carbamate, (1)
N`-(3-hydroxyphenyl)-N`N-dimethylformamidine, (2)
3-formamidophenylmethyl-carbamate, (3)
3-aminophenylmethylcarbamate, (4)
3`-hydroxyformanilide, (5)
3-aminophenol (6)

All are less toxic than formetanate hydrochloride, with LD_{50}-values at least one order of magnitude higher. An *in vitro* study demonstrates that 3-formamidophenylmethylcarbamate (SN 35902) and 3-aminophenylmethylcarbamate (SN 38075) have a lower potential of AChE inhibition. They are not considered toxicologically relevant.

Mechanistic studies:

The kinetics of the AChE inhibition by formetanate hydrochloride were studied in female rats administered a single oral dose by gastric intubation. Plasma and brain AChE activities are significantly depressed one hour after dosing, recovered after 6 hours (except for the high dose). No effect on AChE activity is observed at 0.5 mg/kg bw, the NOAEL. This NOAEL is confirmed in a 28-day AChE activity study in female rats.

The whole blood AChE activity in dogs was also depressed 0.5 to 6 hours after a single oral dose, with complete recovery within 24 hours.

Atropine in female rats was demonstrated to be an effective antidote for formetanate, increasing the LD_{50} of formetanate by a factor 3.

2.9. MEDICAL DATA

No cases of poisonings or other adverse effects were reported during formetanate hydrochloride production in a manufacturing plant, handling of formetanate during Dicarzol manufacturing process, and among agricultural workers using Dicarzol.

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

For the derivation of all the reference values, the safety factor 100 has been applied.

ADI

The ADI is 0.004 mg/kg bw/day, based on the 1-year dog study.

AOEL

The AOEL is 0.004 mg/kg bw/day, based on the 29-day and 1-year dog study.

ARfD

After discussion of the available studies to derive an ARfD, the experts agreed with the first proposal of the rapporteur Member State to base the reference value on the acute study of cholinesterase kinetics in female rats. The resulting ARfD is 0.005 mg/kg bw.

2.11. DERMAL ABSORPTION

An *in vivo* study in male rats was performed with the formulation Dicarzol 500SP (concentrated and diluted), considered equivalent to Dicarzol 500SG by the experts. They agreed that residues remaining in the skin should be included, resulting in a dermal absorption value of 4% for the concentrate and dilutions, instead of the 2% initially proposed by the rapporteur Member State.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Dicarzol 500 SG is a SG formulation containing 500 g formetanate/kg, for use on tomatoes (in field or glasshouse) and ornamental shrubs (in field).

Operator exposure

According to the intended uses submitted by the applicant, the applied dose is 500 g a.s./ha, and the minimum volume 700 L of spray/ha for ornamental shrubs and 800 L of spray/ha for tomatoes. Applications are carried out by tractor mounted equipment, hand held equipment (field) or automated gantry sprayers (glasshouse).

The results of the estimates for the **field use** are in the following table.

Estimated exposure presented as % of AOEL (0.004 mg/kg bw/day), according to calculations with the German model. The default for body weight of operator is 70 kg.

Scenarios	**German model**		
	No PPE	**With PPE***	**With PPE + RPE****
Tractor mounted (20 ha/day)	609	55	nr
Hand held (1ha/day)	496	103	99

* PPE (personal protective equipment): gloves during mixing/loading; gloves, coverall and rubber boots during application.

** RPE (respiratory protective equipment): respiration mask during mixing/loading.

nr : not relevant

The rapporteur Member State has refined the hand held application considering 0.6 ha treated /day in the German and UK models. This approach cannot be considered as fully representative of the worst cases, therefore it can only be taken into account at a MS level.

During **glasshouse use**, no exposure is expected during application because automated glasshouse gantry sprayer is generally remotely operated from control panels outside the treatment area. Thus, significant operator exposure is only expected during mixing and loading via the dermal route, and has been estimated with the German BBA and the UK POEM models (with the use of vehicle mounted equipment).

Estimated exposure presented as % of AOEL (0.004 mg/kg bw/day), according to calculations with the German and UK POEM model. The default for body weight of operator is 70 kg in the German model and 60 kg in the UK-POEM model.

Scenario	**German model**		**UK POEM**	
	No PPE	**With PPE***	**No PPE**	**With PPE***
Automated gantry sprayers (glasshouse)	314	31	833	8.3

* PPE (personal protective equipment): gloves during mixing/loading

This was agreed by the experts. Nevertheless, non automated applications in glasshouse should be taken into consideration at a Member State level.

According to the German model, the estimated operator exposure for formetanate is 55% of the AOEL with PPE for the tractor mounted scenario, and 99% of the AOEL with PPE and RPE for the hand held scenario. According to calculations with UK POEM, application with automated gantry sprayers in glasshouse gives an exposure of 8.3% of the systemic AOEL without PPE.

Worker exposure

The German re-entry model[8], combined with two available DFR (dislodgeable foliar residues) studies has been used for the calculations of worker exposure during tomatoes harvest.

Based on the revised dermal absorption value, the estimated worker exposure would be 10% of the systemic AOEL (for a worker wearing gloves and working 6h/day).

Regarding the application in ornamental shrubbery, there is no exposure expected for the worker because no further handling in the treated area is necessary shortly after application.

Bystander exposure

Based on German drift data[9] for field crop sprayers, the estimated systemic exposure would be 1.1 % of the AOEL, taking into consideration that at a distance of 10 m from the source the drift deposition is 0.29% of the applied dose (90th percentile). Based on a field study conducted in UK[10], the worst case would give an estimated exposure of 1.4 % of the AOEL, assuming a mean potential dermal exposure of 0.1 ml of spray at 8m from the edge of the treatment area.

Knapsack and glasshouse applications are assumed to generate lower exposure levels and are thus of no concern for bystander.

3. Residues

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of formetanate has been investigated in tomatoes, lemons, peaches and alfalfa. These studies cover adequately the representative use on tomatoes and give sufficient information to elucidate the metabolic pathway of formetanate. The extractability of residual compounds is high even for PHIs as long as 90 days after application of the compound. The major constituent of the residue was formetanate in all the investigated crops. The main metabolites found, resulting from the hydrolysis of formetanate were 3-HPDMF, 3-FAPMC and 3-HF, which was found only in the alfalfa metabolism study. These metabolites were present in the rat metabolism, and further more were proved to be at least one order of magnitude less toxic that formetanate (refer to point 2.8). Taking this into account, the toxicological impact of residues resulting from the use of formetanate is essentially due to the parent compound.

Therefore the residue definition for both risk assessment and monitoring is proposed to include the parent compound only. For analytical reasons, as the method of analysis does not distinguish the different salts and the acidic form of formetanate, this residue should be sum of formetanate and its salts, expressed as formetanate hydrochloride.

Supervised residue trials were carried out according to the supported representative uses on glass house and outdoor grown tomatoes (10 trials for both representative uses). The HRs (Highest

[8] Hoenicke *et al*., 1998. Hinweise in der Gebrauchsanleitung zum Schutz von Personen bei Nachfolgearbeiten in mit Pflanzenschutzmitteln behandelten Kulturen. Nachrichtenbl. Deut. Pflanzenschutzd. 50 (10), p 267.

[9] Rautmann et al., 2001

[10] Lloyd and Bell, 1983. Hydraulic nozzles: comparative spray drift study.

Residues) found after a PHI of 14 days were 0.12 and 0.08 mg/kg for indoor and outdoor applications respectively. Respective STMRs (Supervised Trials Median Residues) were 0.09 and 0.04 mg/kg, suggesting that the glasshouse use is critical for the amount of residues at harvest. These results are supported by storage stability studies of formetanate residues on various matrices (tomatoes, apples, stone fruits and citrus fruits) indicating that the compound is stable under deep freeze conditions (-18 to -20°C) for periods ranging from 12 to 33 months.

The effect of processing on the nature of residues was investigated under hydrolysis studies at high temperature simulating pasteurisation, baking, brewing, boiling and sterilisation. 3-HF was identified as the major degradation product of Formetanate following incubation at pH 5/100 °C (simulating boiling) and pH 6/120 °C (simulating sterilisation). Following incubation at pH 4/90°C (simulating pasteurisation) only limited degradation of ^{14}C-Formetanate HCl was evident. The degradation products were 3-HPDMF and 3-FAPMC. These degradation products are similar to those observed in the metabolism studies under natural conditions, and as mentioned here above, their toxicity is significantly lower than that of the parent compound. Their formation during processing does not increase the risk for the consumer and there is no need to establish a specific residue definition for processed commodities. Processing studies were conducted in order to determine transfer factors of formetanate residues from raw tomatoes to processed products. These studies confirmed the results of the hydrolysis studies with a high (0.7) transfer factor to pasteurised tomato juice and low (0.2 and 0.1) transfer factors to sterilised tomato puree and canned tomatoes. Washing leads to reductions of the residue level from 50 to 70 percents.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Although the soil persistence of formetanate and its metabolites is low, a study on the uptake of residues by succeeding crops was carried out. Radish, lettuce and wheat were used as test crops and were sown 30, 120 and 365 days after a 5N soil treatment. Total residues in all plant parts at harvest were generally low, and the organic soluble residues were ranging from 0.01 to 0.1 mg/kg (except in wheat straw where organic soluble residue was close to 0.2 mg/kg). Formetanate was the major identified component. Nevertheless, considering the overdosage factor in the study, it can be estimated that residues of formetanate resulting from soil uptake will not exceed 0.05 mg/kg, and even probably not 0.01 mg/kg.

Therefore no rotational crop MRL or plant back restriction is needed to be established for formetanate.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Although not required as the representative uses of formetanate do not lead to residues in animal feed, metabolism studies in livestock were submitted (dairy cows, lactating goats and laying hens). These studies indicated a rapid absorption, distribution and excretion of residual compounds. The metabolic profile is similar to that observed in rodent metabolism studies. 3-HF was identified as the major metabolite in animal tissues.

As no exposure of livestock is expected to residues of formetanate, no residue definition for animal products is proposed.

3.3. CONSUMER RISK ASSESSMENT

Chronic exposure

The chronic dietary exposure assessment has been carried out according to the WHO guidelines for calculating Theoretical Maximum Daily Intakes (TMDI) and International (National) Estimated Daily intakes (I(N)EDI). Three consumption patterns were considered: the WHO European typical diet for adult consumers, the national Italian diet for adult consumers and the national German diet for a 4-6 year old girl.

The TMDI calculation was conducted for the WHO European diet only, considering the MRL of 0.2 mg/kg proposed for tomatoes. This resulted in a theoretical intake amounting to 5.5% of the ADI.

The I(N)EDI calculations were conducted for the 3 here above mentioned diets, considering residues in tomatoes at the STMR in glass house production (0.09 mg/kg), and without using any processing factor. This resulted in estimated intakes amounting to 2.5, 3.7 and 2.5% of the ADI for the WHO European, Italian and German diets, respectively.

Acute exposure

The acute exposure to residues of formetanate has been assessed according to the WHO model for estimates of short term intakes (NESTI, National Estimated Short Term Intakes). Large portion consumption data for adults, toddlers and infants in UK were used. Calculations were carried out considering residues in treated commodities at the level of the HR residue found in supervised trials (0.12 mg/kg) in glass house conditions (worst case for residue levels) as well as high unit to unit variability factor (7). This resulted in NESTI values close to or above the ARfD for toddlers and infants (99 and 116% of the ARfD respectively). Similar results (110% of the ARfD) were obtained by the EFSA using German consumption data for a 16 kg body weight child. It must be pointed out that the calculations were carried out in line with relevant guidance documents using the highest residue found in supervised trials (0.12 mg/kg) and not the proposed MRL (0.2 mg/kg). This means that residues present at the level of the proposed MRL would represent an exposure clearly above the ARfD for infants and toddlers in case of high unit to unit variability in the analysed sample.

This issue was extensively discussed during the expert meeting (EPCO 29), and a refined calculation based on the highest residue found out of 100 individual tomatoes from a monitoring sample on UK market was provided and considered. This calculation was rejected as the treatment history was not known and for methodological reasons. Beside these reasons it is questionable to the opinion of EFSA if such assessment of the potential acute exposure can rely on one single data set, even containing information on individual units. It is clearly established that the variability is not only depending on the substance, but also on crop, application and environment factors. It was suggested to provide more unit to unit supervised residue data to cover a wide range of possible practical conditions before adopting a specific variability factor for the use of formetanate in tomatoes.

Consideration should also be given to the EFSA opinion[11] adopted on the 16th February 2005 concerning the variability factor.

Further possibilities for refinement of the actual risk for toddlers and infants were also suggested, during the expert meeting (EPCO 29) and the final discussion of the outcome of the consultation of experts, such as the effect of washing or processing on the residue levels. Although it can be expected that residues are significantly reduced by these means and probably reach safe levels, no data from consumption survey are available in the framework of this peer review to exclude the consumption of unwashed raw tomatoes by infants and toddlers. In addendum 3 of January 2006 (not peer-reviewed), the rapporteur Member State submitted new acute intake calculations, taking into account the reducing effect of washing and a lower variability factor of 5, and showing that under these conditions, the exposure of toddlers is well below the ARfD. The decision on whether it is appropriate to take these latest refined calculations under consideration needs to be taken at management level.

Other calculations were conducted during the expert meeting (EPCO 29) on the basis of the residue situation for outdoor grown tomatoes. Using a MRL of 0.1 mg/kg, which could fit to that representative use, it was shown that the potential acute exposure of infants was close to but below the ARfD (97% of the ARfD).

3.4. PROPOSED MRLS

Based on the results of supervised residue trials on tomatoes and their analysis according to statistical tools recommended by current guidelines a MRL of 0.2 mg/kg would be necessary for glass house tomatoes, while a MLR of 0.1 mg/kg could accommodate the outdoor production. However as mentioned here above under point 3.3 the MRL of 0.2 mg/kg for glass house use is questionable in terms of consumer safety.

No MRL is proposed for animal commodities, given that no exposure of livestock is expected from the supported representative uses.

4. Environmental fate and behaviour

The Environmental fate and behaviour in the environment of formetanate was discussed in the experts' meeting (EPCO 26) of June 2005 on basis of the DAR and the addendum 1 to DAR dated May 2005.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

From sterile aqueous hydrolysis studies (see section 4.2.1) it is clear that the hydrolytic breakdown of formetanate is very rapid under alkaline conditions but it is less labile under sterile acidic conditions.

[11] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request from the Commission related to the appropriate variability factor(s) to be used for acute dietary exposure assessment of pesticide residues in fruits and vegetables.

Also formetanate is a basic substance with a pKa of 8.1, so it is protonated at environmentally relevant pH and will exhibit a stronger positive charge under lower soil pH conditions. In alkali soils the extent of protonation will be lower. Thus it might be that formetanate is less bioavailable under acidic soil conditions.

In the available aerobic laboratory degradation studies (25°C, 75% maximum water holding capacity (MWC), 3 soils or 20°C, 40%MWC, 1 soil) where ^{14}C-phenyl-formetanate hydrochloride was dosed a difference in behaviour relating to soil pH is suggested. However the available database is small so it is not possible to make definitive conclusions. A significant route for the sink of the applied radioactivity (AR) was residue not extracted by methanol or water, which accounted for 11.4-85%AR at 49-91 days. When a further methanol Soxhlet extraction was carried out the level of unextracted residues was reduced slightly to 9.2-75.5%AR. An experiment demonstrated that the process of Soxhlet extraction degraded formetanate[12]. Therefore the nature of the Soxhlet extracted soil residue is uncertain, as the Soxhlet extraction procedure has the potential to change the nature of this residue fraction. In these experiments mineralisation to CO_2 accounted for 2.7-79.5%AR (at 49-91 days). The table below provides an indication of the possible difference pH may be having on the pattern of mineralisation and unextracted residues.

Mineralisation and residue extractability of 14C-phenyl formetanate hydrochloride in soils of different pH.

	20°C, pH 5, 1.96 %oc loamy sand	25°C, pH 6.6, 2.5% oc sandy loam	25°C, pH 6.8, 0.79%oc loamy sand	25°C, pH 7.2, 0.94%oc loamy sand
Radioactivity extracted by cold methanol or water (%)	9.1 (91 days)	2.3 (49 days)	2.6 (56 days)	0.8 (59 days)
Radioactivity extracted by cold + Soxhlet extraction (%)	56.9 (91 days)	9.5 (49 days)	8.6(56 days)	3 (59 days)
Non extractable residue (%)	37.4 (91 days)	71.1 (49 days)	75.5 (56 days)	9.2 (59 days)
CO_2 formation (%AR)	2.7 (91 days)	13.7 (49 days)	10.3 (56 days)	79.5 (59 days)

In the non Soxhlet extracts (or cold extracts) from samples taken immediately after application parent formetanate accounted for: 12.9%AR (pH5) 21.5%AR (pH6.6), 44.6%AR (pH6.8) 0%AR (pH 7.2). In these cold extracts the metabolites 3-FAPMC[13], 3-HPDMF[14], 3-HF[15], 3-APMC[16] and 3-AP[17] were present transiently at low levels (max. individual level for a single compound 8.9%AR). When expressed as the sum of cold and Soxhlet extracts the metabolites 3-FAPMC, 3-HF and 3-APMC become major constituents of the residue (up to 20.2, 17.6 and 50.6%AR). The process of Soxhlet

[12] See addendum 2 to the DAR dated November 2005, note the actual study report was peer reviewed at the meeting of experts.
[13] 3-FAPMC: 3-formamidophenyl methylcarbamate
[14] 3-HPDMF: N-(3-hydroxyphenyl)-NN-dimethylformamidine
[15] 3-HF: 3-hydroxyformanilide
[16] 3-APMC: 3-aminophenyl methylcarbamate
[17] 3-AP: 3-aminophenol

extraction may have generated these higher levels of metabolites from precursors in the initially unextracted fraction or they could possibly be present in the soil before extraction. The Member State experts discussed the study designs and the results of the studies and their potential for use in exposure assessment. They agreed that it was possible that all the extracted residue could have been parent formetanate with the breakdown products being extraction artefacts. However they also agreed it could not be excluded that the identified degradation products might really be formed under natural conditions in relatively high amounts. They agreed that it was appropriate to use the studies for exposure assessments and subsequent risk assessments. This agreement was on the proviso that the available exposure assessments covered both the situation assuming all the extractable residue present was formetanate and assuming all the residue was the identified major metabolites. This is the assessment that was available in the DAR.

In anaerobic laboratory degradation studies (2 soils studied) the pattern of breakdown products identified was the same as observed in the studies carried out under aerobic conditions. In laboratory soil photolysis studies on oven dried (120°C) soil, again the pattern of breakdown products identified was the same as observed in the studies carried out under dark aerobic conditions, except the metabolite 3-HPDMF was present at higher concentrations (up to 23%AR at 28 hours). The applicant proposed that in microbially active soils that had not been oven dried, this metabolite would be formed at lower levels as it would be rapidly degraded. Whilst this statement is true, as the degradation rate for 3-HPDMF is relatively slow compared to its rate of formation under photolytic conditions (Peak formation rate in photolysis study 1 day, longest single first order DT_{50} 3.3 days in dark aerobic soils), it cannot be excluded that 3-HPDMF could be formed in microbially active soil at >10%AR. A soil and ground water exposure assessment is therefore pertinent for 3-HPDMF. This is available.

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

Non linear regression single first order DT_{50} were calculated for formetanate from the 25°C 75% MWC aerobic dark laboratory soil degradation studies described in section 4.1.2. above. For the kinetic fit it was assumed that all radioactivity present in Soxhlet extracts was parent formetanate. This residue was added to the levels of formetanate determined in the cold extracts for the 2 acidic soils. For the pH 7.2 soil, even in the cold extracts there was no formetanate present. So for this soil the DT_{50} calculated represents total extractable radioactivity. This resulted in values of 5.97 days (pH7.2), 6.05 days (pH6.6) & 9.66 days (pH6.8) for these 3 soils. After normalising the DT_{50} values in accordance with FOCUS[18] guidance to 20°C and -10kPa soil moisture, the values were 5.97 days (pH7.2), 8.78days (pH6.6) & 12.75days (pH6.8).

In the 2 acidic soils it was possible to use the ModelMaker software to calculate non linear regression first order DT_{50} for the soil metabolites 3-HPDMF (1.5&3.3days), 3-FAPMC (0.64&0.87days), 3-HF

[18] Generic guidance for FOCUS groundwater scenarios Version 1.1 dated April 2002

(0.52&1.0days) and 3-AMPC (0.58&1.9 days) using the residue levels in cold extracts as the basis for the calculations. After normalising the DT_{50} values in accordance with FOCUS guidance to 20°C and -10kPa soil moisture these values were: 3-HPDMF (2.2&4.3days), 3-FAPMC (0.92&1.1days), 3-HF (0.76&1.4days) and 3-AMPC (0.76&2.8 days).

Relied on field dissipation studies were available from two sites in California where the analytical method used, quantified residues of all components of the residue that contain the 3-aminophenol moiety. In these experiments the graphically estimated time for half the initial measured residue containing the 3-aminophenol moiety in the 0-7.6cm soil layer to be reached was about 1 day (pH7.1 soil) and about 9 days (pH 7.8 soil). Note, when the EFSA used single first order non linear regression to calculate the DT_{50}, value at the soil pH 7.8 site, a value of 17.2 days (r^2=0.82) was calculated.

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

In guideline batch soil adsorption studies on 4 soils k_foc of formetanate were in the range 140-620mL/g (Freundlich slope (1/n) 0.81-0.87). To limit the hydrolysis of formetanate over the equilibrium time of the study the pH of the calcium chloride solution was lowered (pH 4-4.5). The pH of all the soils studied were also acidic (pH 5.2-6.4). Based on the fact that at low soil pH formetanate will more strongly protonated (as it is a basic substance with a pKa of 8.1), at higher soil pH conditions than those for which experimental measurement was possible, particularly in alkaline soils, lower adsorption of parent formetanate might be expected? (Under higher soil pH conditions formetanate will be very weakly protonated.) However if this is what occurs, it is unlikely to be of concern for leaching of formetanate in practice, as the effects of lower adsorption would be compensated for by the significantly faster degradation rate that was observed under alkali soil conditions (see section 4.1.2). Some evidence to support this supposition is provided by the results from a soil column leaching study where the soil with the highest pH (6.8) contained the highest proportion of applied radioactivity in leachate (10.7 %), however analysis of the leachate indicated only 3-FAPMC, 3-APMC, 3-HPDMF and 3-HF were present. Formetanate was not present.

Adsorption k_foc and 1/n values for the soil metabolites for 4 soils (except 3-APMC where 3 values are available) were: 68-142mL/g (1/n 0.86-0.91) for 3-FAPMC, 368-1289mL/g (1/n 0.83-0.90) for 3-HPDMF, 253-337mL/g (1/n 0.85-0.91) for 3-HF and 40-70mL/g (1/n 0.66-0.88) for 3-APMC. There was no evidence that the adsorption of the soil metabolites was pH dependant.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

In sterile aqueous hydrolysis studies (20°C) formetanate was very rapidly broken down under alkali conditions (pH9, single first order DT_{50} 2.8 hours) and rapidly broken down under neutral conditions (pH7, single first order DT_{50} 36 hours). Under acidic conditions breakdown was significantly slower

(pH4, single first order DT_{50} 203 days). The major breakdown products were: 3-FAPMC, 3-HPDMF and 3-HF. In a laboratory sterile aqueous photolysis study carried out at pH 5, 7 and 9, the route of degradation apparent was the same as in the dark control / aqueous hydrolysis studies. No novel breakdown products were formed.

In 2 dark aerobic laboratory sediment water systems (20°C, water pH 6.5 and 7.2; sediment pH 6.7 and 7.8) formetanate degraded rapidly to form the major degradation products: 3-FAPMC (max. 34%AR in water at 0.5 days, 4.6%AR in sediment at 3 days), 3-HPDMF (max. 11.6%AR in water at 0.5 days, 4.4%AR in sediment at 1 day), 3-HF (max. 39%AR in water at 7 days, 6.4%AR in sediment at 3 days), 3-APMC (max. 13.5%AR in water at 3 days, 3.3%AR in sediment at 3 days) and 3-AP (max. 23%AR in water at 3 days, 5.5%AR in sediment at 14 days). Residue not extracted from sediment by acidified acetonitrile was a significant sink for the applied radioactivity accounting for 52-58%AR at 28 days. Mineralisation to CO_2 accounted for 14-18 %AR at 28 days increasing in the pH 6.5 system to 30%AR after 70 days. Using a multi compartment model that assumed single first order kinetics between compartments and ModelMaker (v.4) as outlined in detail in addendum 1 to DAR dated May 2005 the DT_{50} values tabulated in appendix 1 (section 1.5) were calculated. All values for parent formetanate were less than 0.6 days with those for the metabolites listed above always being less than 9.3 days (longest value for 3-HF in water)and 17 days (longest value for 3-HF in sediment).

The experts from the Member States considered that there was greater uncertainty in the DT_{50} calculated for the metabolites in this assessment compared to the assessments available for other substances used in plant protection due to the complicated compartment model utilised. However the EFSA considers that this additional uncertainty is acceptable in the aquatic exposure assessment carried out in this case, as the available assessment[19] assumed 100% formation of metabolites in the soil (relating to the drainage and runoff routes of entry) and 100% formation of metabolites in the surface water system. This very conservative assumption would be expected to more than compensate for the acknowledged additional uncertainty in the estimated sediment water system metabolite DT_{50} values. If in the future at the Member State level a less conservative metabolite formation fraction is used in national assessments, a recalculation of metabolite sediment and water DT_{50} values, utilising a more simplified compartment model that had fewer degrees of freedom is recommended by the experts from Member States and the EFSA.

The EFSA has also noted that:

1. the parent formetanate K_foc value (340mL/g mean) used as input to FOCUS surface water modelling will give reasonable worst case sediment PEC but will result in lower time weighted average surface water concentrations being calculated than would have resulted had the arguably (because of indications of pH dependant adsorption) more appropriate lowest K_foc of 140mL/g been used. However as the degradation of formetanate in both surface water and sediment is very rapid, the

[19] That followed FOCUS surface water (SANCO/4802/2001-rev. 2 final (May 2003)) guidance, see section B.8.6.2 of the DAR and addendum 1 to the DAR dated May 2005.

EFSA considers that in this case, for the available EU level assessment, it is not necessary to recalculate the surface water PEC as any difference will be negligible.

2. the available FOCUSsw modelling for the use on ornamental shrubs that used field beans as a surrogate crop in the simulations, used appropriate application dates between mid March and mid July at the different scenarios. Applications were therefore not always simulated at the time of leaf emergence as erroneously stated in Table B.8.64 of the DAR. The available simulations therefore do not cover autumn application timings to ornamental shrubs, as would have been the case at some scenarios had leaf emergence actually been used as the application timing.

3. the necessary PEC surface water have not been calculated for the major water metabolite 3-AP. However as a worst case it is considered the values calculated for 3-HF could be used for the risk assessment (3-HF has a higher molecular weight and longer calculated first order DT_{50}). Note this PEC has not been used in the EU level risk assessment (see section 5.2).

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

FOCUSPELMO 3.3.2. was used to estimate the potential for groundwater contamination by formetanate and its potential soil metabolites 3-FAPMC, 3-HPDMF, 3-HF and 3-APMC under geoclimatic conditions represented by the standard FOCUS groundwater scenarios relating to the applied for intended uses on tomatoes and ornamental plants. The available modelling is described in full in addendum 1 to DAR dated May 2005. Each metabolite was modelled separately assuming an application was made at the soil surface with the metabolite having an application rate calculated as being equivalent to 100% formation from the applied parent compound (a worst case estimate of formation utilised due to uncertainty of the nature of extracted soil residues, see section 4.1.1). Following FOCUS guidance longest laboratory soil DT50 were used as input (12.75 days formetanate, 1.15 days 3-FAPMC, 4.34 days 3-HPDMF, 1.37 days 3-HF and 2.8 days 3-APMC) as only 3 DT_{50} values for formetanate and 2 DT_{50} values for each metabolite were available. The soil adsorption ($K_f$oc) values utilised in the modelling were: 171mL/g 1/n 0.9 (formetanate), 68mL/g 1/n 0.9 (3-FAPMC), 368mL/g 1/n 0.9 (3-HPDMF), 253mL/g 1/n 0.9 (3-HF) and 40mL/g 1/n 0.9 (3-APMC). For the soil metabolites these represent conservative input values as following FOCUS guidance[20] arithmetic mean $K_f$oc and 1/n values (107mL/g 1/n 0.9 (3-FAPMC), 801mL/g 1/n 0.87 (3-HPDMF), 298mL/g 1/n 0.87 (3-HF) and 57mL/g 1/n 0.78 (3-APMC)) representing greater adsorption would have been acceptable. For parent formetanate as there is some indication adsorption may be pH dependant the EFSA proposes the most appropriate values to select would be 140mL/g and 1/n 0.87 from the experiment with an equilibrium time of 4 hours and not the 171mL/g value that came from a study with an equilibrium time of 24 hours.

The outcome of this modelling is that for the applied for intended uses on tomatoes and ornamental plants, annual average leachate concentrations leaving the top 1m soil layer for formetanate and the soil metabolites assessed, are predicted to be less than the parametric drinking water limit for

[20] Generic guidance for FOCUS groundwater scenarios Version 1.1 April 2002.

pesticides of 0.1µg/L (calculated values <0.001µg/L). The EFSA has confirmed that when the slightly less conservative adsorption values for parent formetanate of 140mL/g and 1/n 0.87 are used as modelling input the calculated annual average leachate concentrations remain <0.001µgL. Therefore the potential for groundwater contamination from the applied for intended uses is considered to be minimal.

4.3. FATE AND BEHAVIOUR IN AIR

Formetanate hydrochloride has a vapour pressure of $1.6x10^{-6}$Pa at 25°C and Henry's law constant of $5x10^{-10}$ $Pa.m^3.mol^{-1}$. It would therefore be expected to be essentially non volatile. The very small proportion of the applied active substance that reaches the upper atmosphere would be expected to be degraded as a result of photochemical oxidative degradation based on the Atkinson calculation half life of 1.4 hours. Formetanate is therefore unlikely to subject to long range transport through the atmosphere.

5. Ecotoxicology

Formetanate was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 27) in June 2005. The ecotoxicological studies were conducted with the formulation Dicarzol 500 SP instead of the lead formulation. These two formulations are however considered equal from an ecotoxicological point of view.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk to terrestrial vertebrates was assessed based on the use of 0.5 kg/ha formetanate in tomatoes and ornamental shrubs. In the first tier assessment for birds a medium sized herbivorous bird and a small insectivorous bird in the scenario "leafy crops" were considered in accordance with the Guidance Document on Birds and Mammals (SANCO/4145/2000). The acute toxicity to birds is high, and for the most sensitive species tested, the mallard duck, a LD_{50} of 11.5 mg a.s./kg bw was obtained. The acute TER values are 0.3 for herbivorous birds and 0.4 for insectivorous birds, which is below the Annex VI trigger of 10 and thus indicate a high acute risk. The first tier short-term TERs for the same scenarios are 16.3 and 16.5 respectively (based on LC_{50} in bobwhite quail), and the long-term TERs are 1.9 and 1.0, hence indicating also a long-term risk.

The dietary toxicity endpoint for the short-term assessment was discussed in a meeting with Member State experts. It was proposed that in line with the recommendations in the Guidance Document on Risk Assessment for Birds and Mammals SANCO/4145/2002 the first tier assessment should be based on the lowest $NOEL_{DD}$ from the bobwhite quail or the mallard duck dietary studies instead of the LC_{50} since strong food avoidance was observed in the study with mallards that was the most sensitive species. The TER values calculated based on $NOEL_{DD}$ are 1.5 for both herbivorous and insectivorous birds.

A refined assessment based on measured initial residues and their decline in food items, and refinement of the proportion of different food types in the diet (PD) for the focal species yellow wagtail (*Mocatilla flava*) and wood pigeon (*Columba palumbus*) was presented in addendum 1 (May 2005). Based on these focal species, the long term TERs are 7.4 (wood pigeon) and 16.7 (yellow wagtail) and the long-term risk for this species can thus be considered as low. However, the experts' meeting asked for further justification for the selection of focal species. Such information is given in addendum 2 (October 2005) together with a new refined risk assessment but has not been peer reviewed. Whether the selection of focal species is appropriate should be considered further at Member State level.

The applicant proposed to use the short-term dietary endpoint for the acute assessment instead of the acute LD_{50} obtained by gavage exposure. The arguments given were that birds are eating frequently throughout the day and that the estimated daily intake of formetanate would not occur all at once. Furthermore, it was argued that carbamates are rapidly metabolised and would not lead to any accumulation in the course of a day. The arguments were discussed in the experts' meeting. With regard to use of the dietary endpoint for the acute risk assessment some Member State experts expressed concern. It was agreed to await the opinion of the PPR panel for pirimicarb[21] for which the same approach has been proposed. However, it was noted that the first tier acute TER values were <1. The SETAC/OECD workshop on avian toxicity testing[22] specifically proposed that the avian assessment should be based on the acute oral test when the time quotient is 1 day or less (i.e. TER≤1) and on dietary tests when the time quotient exceeds 1 day (i.e. TER>1).

In addendum 2 it is shown that for yellow wagtail the estimated theoretical exposure (ETE), based on 100% intake of small insects with a RUD based on measured initial residue data, is below the lowest acute LD_{50}, implying that a time quotient approach using the dietary endpoint could be appropriate to assess the acute risk. For wood pigeon a PT factor <0.6 has to be taken into account to obtain ETE below the LD_{50} if based on available worst case data for PD. It should be noted that the TER values are still based on an LC_{50} value obtained from the mallard duck dietary study that was considered unreliable by the expert's meeting due to strong food avoidance. addendum 2 has not been peer reviewed or discussed among Member State experts and a final conclusion can therefore not be drawn at this stage.

For mammals the first tier assessment based on standard generic species indicates a potential acute risk with TER values of 1.7 for medium herbivorous mammals and 4.8 for insectivorous mammals, while it indicates a low long-term risk. The rapporteur Member State proposed refinements based on residue data in different food items, and refinements of PD and PT for brown hare and common shrew as focal species. The assessment was discussed at the experts' meeting and it was concluded that further justification for the choice of focal species and refinements of PD was needed.

[21] http://www.efsa.eu.int/science/ppr/ppr_opinions/1063/ppr_op_ej240_pirimicarb_en1.pdf
[22] OECD (1996). Report of the SETAC/OECD workshop on avian toxicity testing (OECD/GD(96)166, series on testing and assessment n° 5, pp 199.

Refinements of PD should be appropriate to the representative uses. Regarding the refinement of PT the extrapolation from wood mice to shrews was questioned. A justification for the proposed NOAEL for mammals was also required. New acute risk assessments for different focal species are provided in addendum 2 of October 2005. One is based on the wood mice (*Apodemus sylvaticus*) as focal species in tomatoes, taking into account the recommendations given by the PPR Panel in the opinion for pirimicarb. Another one is based on the brown hare (*Lepus europaeus*) as focal species in ornamental shrubs taking into consideration a diet of 100% leafy crops and short grass respectively as a worst case. The relation between LD_{50} and exposure at different proportions of time spent in the area is presented. A similar presentation is given for the common shrew (*Sorex araneus*) as a representative insectivorous mammal based on either a mixed diet or 100% large insects. The assessment provided in addendum 2 has not been peer reviewed.

A justification for the proposed NOAEL is also included in addendum 2. The EFSA agrees with the value of 22.4 mg/kg bw for the ecotoxicological assessment. It should however be noted that the PPR Panel is currently working on an opinion regarding the most appropriate parameter and the most appropriate study to assess the long-term risk to mammals.

No assessment of the risk to birds and mammals due to intake of drinking water was presented in the original DAR but was provided in a revision of addendum 2 (November 2005). However the assessment did only take exposure via open water bodies into account and not puddles and leaf axils as requested by the experts' meeting. Furthermore, the assessment of acute risk to birds was based on the LC_{50} from the dietary toxicity study with Japanese quail in which data on body weight and food intake were missing. An assessment of exposure from puddles or leaf axil reservoirs is presented in addendum 3 (January 2006), however the rapporteur Member State argues that this route of exposure is not relevant for the evaluated uses due to low spray volume and narrow or small leafs. As the log P_{ow} is below 3, formetanate is not likely to bioaccumulate and the risk from secondary poisoning to birds and mammals is considered to be low.

In conclusion the first tier TER values for acute and long term risk to birds were below the trigger indicating a potential risk. Short-term TERs were above the trigger but were based on a LC_{50} value that was questioned by the experts' meeting due to strong food avoidance observed in the study. A refined acute and long-term assessment is available based on measured residues in food items and selected focal species. The assessment has not been peer reviewed or discussed by Member States. It should be noted that the refined acute assessment is based on the questioned LC_{50} value from a short-term dietary study. Also for mammals the first tier assessment indicated a potential acute risk, while the long-term risk was considered low. A refined assessment of the acute risk for different focal species taking recommendations given in the PPR Panel opinions for pirimicarb and metamidophos is available but has not been peer reviewed. Therefore, no final conclusion on the risk to birds and mammals can be reached at this stage.

5.2. RISK TO AQUATIC ORGANISMS

Formetanate is highly toxic to aquatic invertebrates, *Daphnia magna* being the most sensitive of the ten species tested in acute toxicity tests. The EC_{50} determined for *D. magna* is 1.7 µg/L. Fish and algae are less sensitive. The first tier risk assessment indicates an acute and long-term risk to aquatic invertebrates (TER_a=0.1 and TER_{lt}= 1.6) while the risk to fish and algae is low. It should be noted that the long-term TER values in the DAR were calculated based on 21-d TWA PEC in surface water. Since the time to onset of effects is unknown the initial PEC should be used according to SANCO/3268/2001. However, the resulting TER would still be above the Annex VI trigger indicating a low long-term risk to fish.

Results from a microcosm study covering the taxonomic class Rotatoria and the crustacean subclasses Ostracoda, Copepoda and Phyllopoda are available to refine the assessment for aquatic invertebrates. The study was discussed in the experts' meeting and it was agreed that it showed that zooplankton are the most sensitive species and that it was likely that the metabolites would have been present in the microcosm. A NOAEC of 703 µg/L (NOEC for *Daphnia* and increased densities of algae = 38 µg/L) was proposed based on recovery within 8 weeks. The experts' expressed some concern that the recovery of univoltine species was not fully addressed. In addendum 2 of October 2005 the rapporteur Member State presents further arguments for why the results of the microcosm are reliable. The main argument is that based on the results from single species studies it could be concluded that Cladocera represents the clearly most sensitive group and that the univoltine *Cleon* sp. had an EC_{50} 300 times higher than *D. magna*. Furthermore it is argued that the EC_{50} values for the most sensitive non-Cladocera species, *Gammarus* sp. and *Cloeon* sp. are one to two orders of magnitude above the worst case PEC_{sw} calculated based on FOCUS step 3. Also the NOEC values for *Gammarus* sp. and *Cloeon* sp. obtained in the single species tests are one order of magnitude above the calculated PEC_{sw}. Based on the NOAEC from the microcosm a TER value of 54 was calculated indicating a margin of safety for the aquatic invertebrates.

Five metabolites were detected at >10% of applied in the water phase of the water/sediment study. Only for one of them (3-HPDMF) an acute toxicity study with fish is available, which indicates a low toxicity. However, two of the other metabolites (3-FAPMC and 3-APMC) still have the carbamate moiety and a higher toxicity might be expected. The DT_{50} for 3-APMC is 0.3-0.6 days and for 3-FAPMC 1.1-2.2 days. The metabolite 3-FAPMC was detected at 40.8% in the hydrolysis study at pH 7 and could therefore be assumed to have been present in the static toxicity study with formetanate. 3-AMPC on the other hand was only detected in the water/sediment study and it can therefore not be assumed that it was tested with the parent substance. However, since *Daphnia magna* is several orders of magnitude more sensitive to formetanate than fish, the risk assessment is driven by tests with invertebrates and it is the EFSA opinion that no further testing on fish is required. Only formetanate, but none of the metabolites were detected above 10% in the sediment phase of the water/sediment study. The effects on sediment dwelling organisms are assumed to have been tested in the microcosm study.

Since formetanate degrades rapidly in water and the log P_{ow} is <3 a bioconcentration study is not required. However, a study is available and the results is a bioconcentration factor <1. Only one of the metabolites (3-HF) detected in the water/sediment study has a DT_{90} >10 days. The log P_{ow} was calculated to -0.67 and the potential for bioaccumulation is therefore considered negligible.

5.3. RISK TO BEES

Bees may be exposed to formetanate by over spraying, by ingestion of contaminated nectar and honey dew and by contact with residues on plants. The HQ values obtained based on first tier oral and contact toxicity studies clearly indicate a high risk. Based on the results from a cage test where no significant effects in bee mortality or flight intensity was observed after exposure to 14-day aged residues on flowering *Phacelia*, the experts' meeting concluded that if formetanate is applied two weeks prior to flowering the risk to bees should be low.

5.4. RISK TO OTHER ARTHROPOD SPECIES

The first tier risk assessment based on laboratory data for the standard species *Aphidius rhopalosiphi* and *Thyphlodromus pyri* indicates a high risk to non-target arthropods. Extended laboratory tests are available with *A. rhopalosiphi* and two additional species, *Chrysoperla carnea* and *Coccinella septempunctata*. No mortality or sublethal effects were observed for *C. septempunctata* at 1000 g a.s./ha. For *C. carnea* 48% mortality was observed at 50 mg a.s./ha but no significant sublethal effects. Mortality of 66.7% was observed for *A. rhopalosiphi* in the extended laboratory study at a test concentration corresponding to a drift rate at 50 m distance from the field, taking a safety factor of 5 for species sensitivity variation into account. An aged residue study with the most sensitive species, *A. rhopalosiphi*, was used to demonstrate potential for recolonisation. After 35 days ageing of residues applied at 500 g a.s./ha 20% mortality was observed. Even though this shows a potential for recolonisation of the treated field, the effects on sensitive arthropods far off the field border are high and the potential for recolonisation and recovery therefore low. Further data is therefore considered necessary to fully address the impact off-field, and the potential for recolonisation. Furthermore, an extended laboratory study or other higher tier study with *T. pyri* is lacking and it was decided in the experts' meting that such a study is required in order to fully assess the off-field risk and potential for recolonisation and recovery.

5.5. RISK TO EARTHWORMS

A study on the acute toxicity to earthworms from formetanate indicates a low toxicity. The acute TER value is 3147 and therefore the acute risk to earthworms is considered to be low. The long term TER is 5.4, which is slightly above the Annex VI trigger of 5 and thus no further studies are required.

No studies are available with the three major soil metabolites detected after aerobic degradation or the photolysis metabolite. The experts' meeting concluded that the metabolites are short lived in soil but that it is not known whether they were present in the long-term earthworm study. The rapporteur Member State argues in the revised addendum 2 (November 2005) that formetanate is hydrolytically

degraded and that it can be assumed that the metabolites were present in the earthworm study since the soil moisture is adjusted to 40-60% MHC. This argumentation has not been peer reviewed, but the EFSA agrees that 3-FAPMC and 3-HF were probably present. However, 3-APMC was only detected in the aerobic soil degradation study. In addendum 3 of January 2006 (not peer reviewed) the rapporteur Member State provides a long-term assessment for 3-APMC assuming the same toxicity as for formetanate and a formation rate of 100%. The resulting TER is 8.6. Considering the short half-life in soil and the high acute TER value for formetanate, the EFSA agrees to the rapporteur Member State conclusion of low risk to earthworms from exposure to 3-APMC.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

No data is available and not considered necessary since formetanate and its degradation products dissipates fast in soil.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of formetanate on soil carbon and nitrogen conversion were tested using the formulation Dicarzol 500 SP. Transient effects were observed on nitrate concentration. However, no deviations of more than 25% after 28 days were observed at dose rates 5 times the recommended application rate. Hence the Annex VI trigger was met indicating a low risk.

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

No signs of phytotoxicity were observed in a vegetative vigour test with 10 different species using Dicarzol 500 SP at 0.5 kg a.s./ha indicating that the risk to non-target plants is low.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

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

6. Residue definitions

Soil

Definitions for risk assessment: formetanate, 3-Formamidophenyl methylcarbamate, 3-Aminophenyl methylcarbamate, N'-(3-hydroxyphenyl)-N'N-dimethylformamidine, 3-hydroxyformanilide

Definitions for monitoring: formetanate and its salts

Water

Ground water

Definitions for exposure assessment: formetanate, 3-Formamidophenyl methylcarbamate, 3-Aminophenyl methylcarbamate, N'-(3-hydroxyphenyl)-N'N-dimethylformamidine, 3-hydroxyformanilide

Definitions for monitoring: formetanate and its salts

Surface water

Definitions for risk assessment: water: formetanate, 3-Formamidophenyl methylcarbamate, 3-Aminophenyl methylcarbamate, N'-(3-hydroxyphenyl)-N'N-dimethylformamidine, 3-hydroxyformanilide, 3-aminophenol,

sediment: formetanate

Definitions for monitoring: formetanate and its salts

Air

Definitions for risk assessment: formetanate

Definitions for monitoring: formetanate

Food of plant origin

Definitions for risk assessment: sum of formetanate and its salts, expressed as formetanate (hydrochloride)

Definitions for monitoring: sum of formetanate and its salts, expressed as formetanate (hydrochloride)

Food of animal origin

Definitions for risk assessment: no residue definition proposed as no expected exposure of livestock

Definitions for monitoring: no residue definition proposed as no expected exposure of livestock

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
formetanate,	low to moderate persistence ($DT_{50\ lab}$ = 6-12.7 d, 20°C, -10kPa soil moisture)	See sections 5.5, 5.6 and 5.7
3-Formamidophenyl methylcarbamate,	Very low persistence ($DT_{50\ lab}$ = 0.9-1.1 d, 20°C, -10kPa soil moisture)	No studies available. Short-lived hydrolysis product at pH 7 and probably present in the earthworm study with formetanate.
3-Aminophenyl methylcarbamate,	Very low to low persistence ($DT_{50\ lab}$ = 0.76-2.8 d, 20°C, -10kPa soil moisture)	No studies available. Detected only in aerobic degradation study and can therefore not be concluded to have been present in the earthworm study with formetanate. The risk needs to be further addressed.
N'-(3-hydroxyphenyl)-N'N-dimethylformamidine	low persistence ($DT_{50\ lab}$ = 2.2-4.3 d, 20°C, -10kPa soil moisture)	No studies available. Short-lived hydrolysis product at pH 7 and probably present in the earthworm study with formetanate.
3-hydroxyformanilide	Very low to low persistence ($DT_{50\ lab}$ = 0.76-1.4 d, 20°C, -10kPa soil moisture)	No studies available. Short-lived hydrolysis product at pH 7 and probably present in the test system with formetanate.

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
formetanate,	high to low mobility (Koc = 140-620 mL/g) Potential pH dependance	No	Yes	Yes	Yes
3-Formamidophenyl methylcarbamate,	high mobility (Koc = 68-142 mL/g)	No	No exposure. No assessment needed.	No oral LD_{50} 327 mg/kg bw	No exposure. No assessment needed.
3-Aminophenyl methylcarbamate,	Very high to high mobility (Koc = 40-70 mL/g)	No	No exposure. No assessment needed.	No oral LD_{50} 218 mg/kg bw	No exposure. No assessment needed.
N'-(3-hydroxyphenyl)-N'N-dimethylformamidine,	medium to low mobility (Koc = 368-1289 mL/g)	No	No exposure. No assessment needed.	No oral LD_{50} 400 mg/kg bw	No exposure. No assessment needed.
3-hydroxyformanilide	medium mobility (Koc = 253-337 mL/g)	No	No exposure. No assessment needed.	No oral LD_{50} 1830 mg/kg bw	No exposure. No assessment needed.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
formetanate,	See section 5.2
3-Formamidophenyl methylcarbamate,	Assumed to have been present in static fish acute toxicity study with formetanate. Assumed to have been present and assessed in microcosm study with formetanate.
3-Aminophenyl methylcarbamate,	Assumed to have been present and assessed in microcosm study with formetanate. No study with fish available but since formetanate is several orders of magnitude more toxic to Daphnids than to fish this is assumed to be true also for the metabolite.
N'-(3-hydroxyphenyl)-N'N-dimethylformamidine,	Low acute toxicity to fish. Assumed to have been present and assessed in microcosm study with formetanate.
3-hydroxyformanilide	Assumed to have been present and assessed in microcosm study with formetanate. No study with fish available but since formetanate is several orders of magnitude more toxic to Daphnids than to fish this is assumed to be true also for the metabolite.
3-aminophenol.	Assumed to have been present and assessed in microcosm study with formetanate. No study with fish available but since formetanate is several orders of magnitude more toxic to Daphnids than to fish this is assumed to be true also for the metabolite.

Air

Compound (name and/or code)	Toxicology
formetanate	Highly toxic by inhalation (LC_{50} 0.15 mg/L)

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

- Data on the identity of one unknown impurity ("no. 2" of the six unknown) (the rapporteur Member State has received a study but not evaluated it, March 2006, data gap identified at the evaluation meeting and confirmed by the expert meeting, refer to chapter 1).
- Clarification with respect to the proposed specification for the maximum levels of certain impurities in the technical material (data gap identified by the expert meeting; refer to chapter 1; the rapporteur Member State has received (November 2005) a new specification, but has not evaluated it).
- A shelf-life study (data gap identified at the evaluation meeting and confirmed by the expert meeting, the rapporteur Member State has received a study (November 2005), but has not evaluated it; refer to chapter 1).
- Unit to unit residue data addressing a representative range of practical conditions of use of formetanate on tomatoes grown in glasshouse in order to refine the variability factor to be used in acute exposure assessment (relevant for glass house tomatoes; data gap identified by the expert meeting; submission date unknown; refer to point 3.3).
- Refined information on the form (raw or processed) tomatoes are consumed by young consumers (infants, toddlers) (relevant for glass house tomatoes; data gap identified by the expert meeting; submission date unknown; refer to point 3.3).
- The risk to birds has to be further addressed, including the risk from exposure via contaminated drinking water (relevant for outdoor use in tomatoes and ornamental shrubs; refined assessments are available in addendum 2 of October 2005 and addendum 3 of January 2006 but have not been peer reviewed; refer to point 5.1).
- The acute risk to mammals has to be further addressed, including the risk from exposure via contaminated drinking water (relevant for outdoor use in tomatoes and ornamental shrubs; a refined assessment is available in addendum 2 of October 2005 but has not been peer reviewed; refer to point 5.1).
- The risk to non-target arthropods off-field and the potential for recolonisation and recovery needs to be further addressed by means of semi-field or field studies with a sufficient number of species (relevant for outdoor use in tomatoes and ornamental shrubs; submission date unknown; refer to point 5.4).
- An higher tier study with *Thyphlodromus pyri* is required to fully assess the risk to non-target arthropods (relevant for outdoor use in tomatoes and ornamental shrubs; submission indicated for end of 2006; refer to point 5.4).
- The acute risk to earthworms from the soil metabolite 3-APMC needs to be further addressed (relevant for outdoor use in tomatoes and ornamental shrubs; data gap identified during drafting of EFSA conclusion report; assessment available in addendum 3 of January 2006 (not peer reviewed); refer to point 5.5).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as acaricide and insecticide comprise broadcast spraying to control the thrips and mites in tomatoes and ornamental shrubs at an application rate of 500 g formetanate per hectare. Formetanate can be as acaricide and insecticide.

The representative formulated product for the evaluation was "Dicarzol 500 SG" ("AEB036056 00 SG58 A200"), a water soluble granule (SG), registered in France, Portugal and Spain.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. formetanate and its salts in food of plant origin, soil and water.

In the case of air it should be noted that the analytical method is not specific as required in, because it is not possible to differentiate between residue of formetanate and its salts.

Also an analytical method for blood (plasma) is available to cover Annex point 4.2.5 of Directive 96/46/EC.

Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

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

Formetanate hydrochloride is rapidly and extensively absorbed after oral administration. It is mainly excreted in urine. No tendency for bioaccumulation was observed.

It is highly toxic after oral administration and by inhalation, not toxic after dermal exposure, not irritant, but a skin sensitizer. The proposed classification is: **T^+, R26/28 "Highly toxic by inhalation and if swallowed"; Xi, R43 "May cause sensitisation by skin contact"**.

Short term toxicity is manifested by cholinesterase inhibition in all species, the dog being the most sensitive. Formetanate hydrochloride has a mutagenic potential in vitro, but not in vivo, and there is no evidence of carcinogenicity in rats and mice. No reproductive or teratogenic effects have been observed in rats and rabbits. All the tested metabolites are less toxic than formetanate hydrochloride. The kinetics of cholinesterase inhibition was studied in female rats and in dogs.

The Acceptable Daily Intake (ADI) is 0.004 mg/kg bw/day, the Acceptable Operator Exposure Level (AOEL) is 0.004 mg/kg bw/day, and the Acute Reference Dose (ARfD) is 0.005 mg/kg bw. All the reference values were derived with a safety factor of 100.

According to the German model, the estimated operator exposure during field use is 55% of the AOEL with PPE for the tractor mounted scenario, and 99% of the AOEL with PPE and RPE for the hand held scenario. According to calculations with the German and UK models, application with automated gantry sprayers in glasshouse gives an operator exposure of 31 and 8.3% of the systemic AOEL with PPE. The worker exposure (during tomatoes harvest) and the bystander exposure estimates are below the AOEL.

The metabolism of formetanate has been fully elucidated and proceeds through hydrolysis steps. The parent compound has been identified as the major constituent of the residue on various crops and for various PHIs. The identified metabolites are less toxic than the parent compound. Therefore the residue definition can be restricted to parent compound only, for both risk assessment and monitoring. Under processing, formetanate is degraded at temperature of 100°C or higher to a less toxic compound, 3-hydroxyformanilide. The processed commodities obtained after boiling or sterilisation have a significantly lower concentration of formetanate than raw tomatoes.
There is no exposure of livestock to formetanate residues. The soil uptake by rotational crops is minimal and there is no need for setting plant back restriction.
The chronic exposure of the consumer is well below the ADI of formetanate.
Acute intake calculations have indicated a potential acute risk for infants and toddlers resulting from the consumption of treated tomatoes grown under glass house conditions. The level of the proposed MRL in tomatoes, which is significantly higher than the level considered in exposure assessments, causes still higher concerns in terms of consumer safety.

The information available on the fate and behaviour in the environment is sufficient to carry out an appropriate environmental exposure assessment at the EU level. For the notified intended uses, the potential for groundwater exposure by formetanate or its potential soil metabolites 3-FAPMC, 3-HPDMF, 3-HF and 3-APMC above the parametric drinking water limit of 0.1µg/L, is considered low.

The first tier risk assessment for birds indicates acute and long term risk to birds. Short-term TERs were above the trigger but were based on a LC_{50} value that was questioned by the experts' meeting due to strong food avoidance observed in the study. A refined acute and long-term assessment is available based on measured residues in food items and selected focal species. Due to the late submission date this assessment has not been peer reviewed or discussed by Member States. It should be noted that the refined acute assessment is based on the questioned LC_{50} value from a short-term dietary study. Also for mammals the first tier assessment indicated an acute risk, while the long-term risk was considered low. A refined assessment of the acute risk for different focal species taking recommendations given in the PPR Panel opinions for pirimicarb and metamidophos into account is available but has not been peer reviewed. Therefore, no final conclusion on the risk to birds and mammals can be reached at this stage. Formetanate is very toxic to aquatic invertebrates, particularly cladocerans. Based on the results from an available microcosm study the risk is however considered to be low for the evaluated representative uses. Toxicity towards bees and other non-target arthropods is high. Formetanate should not be applied later than two weeks before flowering to protect bees. Even though a potential for in-field recolonisation has been demonstrated, the risk to sensitive non-target arthropods off-field is high even at a distance of 50 m from the field border. Further data is required to fully address the impact off-field and the potential for recolonisation. Furthermore a higher tier study with *T. pyri* is required. The risk to earthworms, other soil macro- and micro-organisms, flora and biological methods of sewage treatment is considered as low.

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

- PPE are necessary to reduce the operator exposure (refer to point 2.12).
- Formetanate is toxic to bees and should not be applied later than two weeks before flowering. (refer to point 5.3).

Critical areas of concern

- At the moment no final specification can be set for the technical material with respect to the maximum content of certain impurities.
- With the available analytical method for the determination of residues in air it is not possible to distinguish between residues of formetanate and of its salts.
- Very toxic orally and by inhalation.
- In glasshouse, only operator exposure during the use of automated gantry sprayers has been assessed.
- The estimated operator exposure during hand-held application in the field is close to the AOEL value (99%) even with the use of RPE in addition to PPE (gloves, coverall and boots).
- An acute dietary risk for infants and toddlers consuming unwashed tomatoes grown under glass house conditions is expected as the ARfD is exceeded for some consumption patterns.
- The level of the proposed MRL for tomatoes grown under glass house conditions, which is almost 2 times higher the highest residue level in field trials in critical conditions, causes concern in terms of consumer safety. The acute exposure of infants and toddlers will clearly exceed the ARfD for samples in compliance with the proposed MRL but with high unit to unit variability of residues.
- The first tier assessment indicated a high acute, short and long term risk to birds. A refined assessment is available but has not been peer reviewed.
- The first tier assessment indicated a high acute risk to mammals. A refined assessment is available but has not been peer reviewed.
- The risk to bees is high. Formetanate should not be applied later than two weeks before flowering.
- The risk to non-target arthropods is high even at a distance of 50 m from the field border.

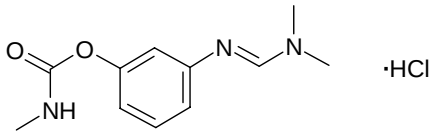
APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

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

Active substance (ISO Common Name) ‡	Formetanate (unless otherwise stated, the following data relate to the variant formetanate hydrochloride)
Function (e.g. fungicide)	Acaricide and insecticide
Rapporteur Member State	Italy
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	3-dimethylaminomethyleneaminophenyl methylcarbamate hydrochloride
Chemical name (CA) ‡	*N*,*N*-dimethyl-*N´*-[3-[[(methylamino)carbonyl]oxy]phenyl] methanimidamide hydrochloride
CIPAC No ‡	697 (formetanate) 697.601 (formetanate hydrochloride)
CAS No ‡	23422-53-9
EEC No (EINECS or ELINCS) ‡	245-656-0
FAO Specification ‡ (including year of publication)	Not available
Minimum purity of the active substance as manufactured ‡ (g/kg)	910 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None
Molecular formula ‡	$C_{11}H_{16}ClN_3O_2$
Molecular mass ‡	257.8
Structural formula ‡	

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

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	193-199 °C (purity 98.3%)
Boiling point (state purity) ‡	Not determinable: the test substance decomposes after melting (purity 98.3%)
Temperature of decomposition	>204 °C (purity 98.3%)
Appearance (state purity) ‡	Fine homogenous powder (technical grade)
Relative density (state purity) ‡	1.18 at 20 °C (purity 98.3%)
Surface tension	70.5 mN/m^{-1} at 20 °C (purity 91.3%; 1g/L solution) test concentration : 1 g/L
Vapour pressure (in Pa, state temperature) ‡	1.6×10^{-6} Pa (25 °C) (purity 99.5%)
Henry's law constant (Pa m^3 mol^{-1}) ‡	5×10^{-10} Pa × m^3 × mol^{-1}
Solubility in water ‡ (g/l or mg/l, state temperature)	822 g/L at 25 °C (in bidistilled water) (purity 98%) pH 4: > 500 g/l at 20 °C pH10: 13.8 g/l at 20 °C (measured after 30 min due to the fast hydrolytical degradation) (purity 98.3%)
Solubility in organic solvents ‡ (in g/l or mg/l, state temperature)	Solubility at 20 °C in: *n*-hexan < 0.0005 g/L methanol 283 g/L dichloromethane 0.303 g/L toluene 0.010 g/L acetone 0.074 g/L ethyl acetate 0.001 g/L
Partition co-efficient (log POW) ‡ (state pH and temperature)	pH 4: logPow = -1.03 (20 °C) pH 7: logPow = -0.0014 (20 °C) pH 10: logPow = 0.83 (20 °C) (purity 98.3%)
Hydrolytic stability (DT50) ‡ (state pH and temperature)	pH 5 (22 °C): DT_{50} = 1500 h (62.5 days) ; kobs = 4.63 × 10-4 [h]-1 pH 7 (22 °C): DT_{50} = 23 h, kobs = 3.05 × 10-2 [h]-1 pH 9 (22 °C): DT_{50} = 2 h, kobs = 3.47 10-1 [h]-1 Main hydrolytic product: 3-hydroxy-phenyl formamide

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

	pH 4 (20 °C): DT_{50} = 203 days pH 7 (20 °C): DT_{50} = 36.3 h, pH 9 (20 °C): DT_{50} = 2.84 h. Main hydrolytic products: 3-formylaminophenyl methylcarbamate and 3-dimethylamino-methylene-amino-phenol.
Dissociation constant ‡	pKa = 8.1 at 25 °C (purity 98.3%)
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	Max. Molecular absorption: In CH3OH ε (L.mol-1.cm-1) = 20400 at 211 nm ε (L.mol-1.cm-1) = 1516 at 252 nm; In 0.1 M NaOH in CH3OH/H2O: ε (L.mol-1.cm-1) = 21000 at 236 nm ε (L.mol-1.cm-1) = 9370 at 267 nm (shoulder) ε (L.mol-1.cm-1) = 5960 at 294 nm (shoulder)
	Purified water (pH 7): ε (L.mol-1.cm-1) = 21400 at 208 nm: ε (L.mol-1.cm-1) = 16400 at 251 nm 0.1 M Hydrochloric acid (pH 1.2): ε (L.mol-1.cm-1) = 21500 at 208 nm ε (L.mol-1.cm-1) = 16400 at 250 nm 0.1 M Sodium hydroxide (pH 13.1): ε (L.mol-1.cm-1) = 21800 at 238 nm ε (L.mol-1.cm-1) = 11000 at 265 nm ε (L.mol-1.cm-1) = 6670 at 295 nm
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	pH 5 DT_{50}: 1333.0 [h]; (55.54 days), Rate constant: 0.0005 [h-1]; pH 7 DT_{50}: 17.0 [h], Rate constant: 0.041 [h-1]; pH 9 DT_{50}: 2.9 [h], Rate constant: 0.240 [h-1] Degradation observed at each pH value was due to hydrolysis and not to photolysis

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

Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	Not calculated – Justification given: the degradation observed at each pH value was due to hydrolysis and not to photolysis
Flammability ‡	Not flammable (purity 91.3%)
Explosive properties ‡	Not explosive (purity 91.3%)

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

List of representative uses evaluated*

Crop and/or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
(a)			(b)	(c)	Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j,o)	number min max (k)	interval between applications (min)	kg a.s./hl min max	water l/ha min max	kg a.s./ha min max	(l)	(m)
Tomatoes	SE	Dicarzol (SG 500 g/kg)	F	Biting and sucking insects	SG	500 g/kg	Spraying	nr	1	nr	0.04 - 0.06	800 - 1200	0.5	14	[1]
Tomatoes	Europe	Dicarzol (SG 500 g/kg)	G	Biting and sucking insects	SG	500 g/kg	Spraying	nr	1	nr	0.04 - 0.06	800 - 1200	0.5	14	[2]
Ornamental shrubs	Europe	Dicarzol (SG 500 g/kg)	F	Biting and sucking insects	SG	500 g/kg	Spraying	nr	1	nr	0.06 - 0.07	700 - 800	0.5	nr	[1]

[1] The risk assessment has revealed a risk in section 5 and due to data gaps other risk assessments cannot be concluded.
[2] An acute dietary risk for infants and toddlers consuming unwashed tomatoes grown under glass has been identified in section 3.

Remarks:				
	*	Uses for which risk assessment could not been concluded due to lack of essential data are marked grey	(h)	Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
	(a)	For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)	(i)	g/kg or g/L
	(b)	Outdoor or field use (F), glasshouse application (G) or indoor application (I)	(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
	(c)	*e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds		
	(d)	*e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)	(k)	The minimum and maximum number of application possible under practical conditions of use must be provided
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989		
	(f)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench	(l)	PHI - minimum pre-harvest interval
	(g)	All abbreviations used must be explained	(m)	Remarks may include: Extent of use/economic importance/restrictions

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

Appendix 1.2: Methods of Analysis

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

Technical as (principle of method)	HPLC – UV
Impurities in technical as (principle of method)	HPLC – UV and GC – FID
Plant protection product (principle of method)	HPLC – UV

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	LC-MS/MS (LOQ = 0.005 mg/Kg) Tomato and processed commodities Due to the extraction procedure, the method does not discriminate between formetanate and formetanate HCl
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	A residue definition has not to be proposed for animal products and therefore an analytical method for the determination of Formetanate residues in products of animal origin is not necessary
Soil (principle of method and LOQ)	LC-MS/MS (LOQ 0.05 mg/kg) Due to the extraction procedure, the method does not discriminate between formetanate and formetanate HCl
Water (principle of method and LOQ)	LC-MS/MS (LOQ 0.05 µg/L) Drinking, ground and surface water
Air (principle of method and LOQ)	LC-MS/MS (LOQ 1.11 x 10^{-7} mg/L air) Due to the extraction procedure, the method does not discriminate between formetanate and formetanate HCl
Body fluids and tissues (principle of method and LOQ)	LC-MS/MS human plasma and urines (LOQ 0.05 mg/L) pig liver (LOQ 0.1 mg/kg)

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	None

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

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Rapidly absorbed (> 96% at 120 hours) at single (low and high dose) and repeated dose based on urinary excretion including a comparison of oral vs i.v. dosing (rat)
Distribution ‡	Readily distributed in body tissues, with highest levels in the liver
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	> 92% urine (predominately during the first 24 hours) about 4% faeces (predominately during the first 24 hours)
Metabolism in animals ‡	Extensively metabolised. Major pathways: - cleavage from the amino nitrogen and removal of N-methylcarbamate resulting in 3`Hydroxyformanilide - deformylation of 3`Hydroxyformanilide to 3-Aminophenol and acetylation of the amino group
Toxicologically significant compounds ‡ (animals, plants and environment)	Formetanate

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	14.8 mg/kg bw	**R28**
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	
Rat LC_{50} inhalation ‡	0.15 mg/L (snout only)	**R26**
Rat LC_{50} inhalation ‡	0.29 mg/L (whole body)	
Skin irritation (0.5 g)‡	Not irritant	
Eye irritation (0.1 mLeg. to 0.43 mg)‡	Not irritant	
Skin sensitization ‡ (test method used and result)	Sensitising properties (Modified Buehler test; 9 applications)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Cholinesterase inhibition (RBC, plasma and brain)
Lowest relevant oral NOAEL / NOEL ‡	0.4 mg/kg bw (29 day and 1 year study in dogs)
Lowest relevant dermal NOAEL / NOEL ‡	20 mg/kg bw (21 day study in rats)

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

Lowest relevant inhalation NOAEL / NOEL ‡	No data – not required

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	No genotoxic potential.

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

Target/critical effect ‡	Cholinesterase (whole blood, plasma, brain)
Lowest relevant NOAEL / NOEL ‡	2.3 mg/kg bw/day (male rats)
Carcinogenicity ‡	No indication of a carcinogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Reduced body weight and decreased viability index of F2a and F2b-offspring at parental toxic doses. ChE inhibition and reduced BWG in parents.
Lowest relevant reproductive NOAEL / NOEL ‡	parental and offspring: 4.5 mg/kg bw/day reproductive: 22 mg/kg bw/day
Developmental target / critical effect ‡	No treatment related effect on developmental parameter at the highest dose tested (5 mg/kg bw/day). Reduced maternal body weight gain.
Lowest relevant developmental NOAEL / NOEL ‡	maternal: 1 mg/kg bw/day embryofoetal: > 5 mg/kg bw/day (rat)

Neurotoxicity / Delayed neurotoxicity ‡ (Annex IIA, point 5.7)

.....	No potential to induce delayed neurotoxicity in hens Acute neurotoxicity (by gavage): NOAEL for ChE inhibition: 0.1 mg/kg bw, LOAEL: 1 mg/kg bw. Subchronic dietary neurotoxicity: NOAEL for ChE inhibition: 18.4 mg/kg bw/day in males

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

Other toxicological studies ‡ (Annex IIA, point 5.8)

Kinetics of the ChE inhibition by formetanate hydrochloride	Overall values for the supplemental studies: NOAEL for brain ChE: 0.5 mg/kg bw/day LOAEL for brain ChE: 2 mg/kg bw/day
Metabolites	All metabolites tested orally were less toxic than the parent compound. Two were tested in vitro, and showed a lower cholinesterase inhibiting potential than the parent compound.

Medical data ‡ (Annex IIA, point 5.9)

.....	No detrimental effects on the health of workers involved in the manufacture of Formetanate

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.004 mg/kg bw/day	1 year study dog	100
AOEL ‡	0.004 mg/kg bw/day	1 year study dog and 29-d study dog	100
ARfD ‡ (acute reference dose)	0.005 mg/kg bw	acute cholinesterase kinetics studies in rats	100

Dermal absorption (Annex IIIA, point 7.3)

Dicarzol 500SP, equivalent to Dicarzol 500SG	4% for concentrate and dilution, in vivo rat with formetanate hydrochloride

Acceptable exposure scenarios (including method of calculation)

Operator

Estimated exposures in % of AOEL are:
- in the tractor mounted scenario:

	no PPE	PPE	PPE + RPE
German	609	55	-

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

	- in the hand held scenario:			
		no PPE	PPE	PPE + RPE
	German	496	103	99
	- in the glasshouse scenario:			
	German	314	31	-
	UK POEM	833	8.3	-
Workers	Exposure is 10% of the AOEL with the use of gloves (BBA re-entry model)			
Bystanders	No risk identified for proposed uses without PPE (up to 1.4% of the AOEL)			

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	T+, Very toxic
	R26/28 Very toxic by inhalation and if swallowed
	Xi, R43 May cause sensitisation by skin contact

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

Appendix 1.4: Residues

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

Plant groups covered	Fruits (tomatoes, lemons, peaches), leafy crops (alfalfa)
Rotational crops	Wheat, lettuce and radish
Plant residue definition for monitoring	Sum of formetanate and its salts expressed as Formetanate (hydrochloride)
Plant residue definition for risk assessment	Sum of formetanate and its salts expressed as Formetanate (hydrochloride)
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	Lactating ruminant (cow, goat), poultry (laying hen)
Animal residue definition for monitoring	Not required
Animal residue definition for risk assessment	Not required
Conversion factor (monitoring to risk assessment)	Not required
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Not required

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

.....	Rotational Crops Study with ^{14}C-Formetanate using wheat, lettuce, and radish available, although according to half-life in soil (6-9 days) not triggered

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

.....	Formetanate in water-containing plant materials stable for periods of storage at –20°C for at least 12 months

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

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: no	Poultry: no	Pig: no
Muscle Liver Kidney Fat Milk Eggs	No feeling study required		

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

Summary of critical residues data (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP mg formetanate/kg (a)	Recommendation/comments	Proposed MRL	STMR (b)
Tomatoes (outdoor)	Southern Europe	1 x 0.01, 1 x 0.02, 3 x 0.03, 1 x 0.04, 2 x 0.05, 1 x 0.06, 1 x 0.08	trials according to GAP	0.1	0.04
Tomatoes (glasshouse)	Europe	1 x 0.05, 2 x 0.07, 1 x 0.08, 2 x 0.09, 1 x 0.10, 3 x 0.12	trials according to GAP	0.2	0.09

(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 critical GAP

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

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

ADI	0.004 mg/kg bw/d	
TMDI (European Diet) (% ADI)	5.5 %	
NEDI (% ADI)	2.5 % (WHO European diet), 3.7 % (Italy), 2.5 % (Germany)	
Factors included in NEDI	STMR	
ARfD	0.005 mg/kg bw/d	
Acute exposure (% ARfD)	Glass house tomatoes: 99% Toddlers UK 116% Infants UK 110% Toddlers DE Outdoor tomatoes: 77% Infants UK	Glass house tomatoes: 165% Toddlers UK 193% Infants UK 184% Toddlers DE Outdoor tomatoes: 97% Infants UK
Factors included in NESTI	HR, variability factor 7	MRL, variability factor 7

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

Crop/processed crop	Number of studies	Transfer factor	% Transference*
Tomatoes after washing	2	0.4	44
Tomato juice processing			
Tomato juice (after pasteurisation/packaging)	4	0.72	37.05
Ketchup processing			
Ketchup (after sterilisation)	4	0.22	2.35
Tomato puree processing			
Tomato puree (after sterilisation)	4	0.19	0.89
Canned tomato processing			
Canned whole tomatoes (after sterilisation)	4	0.17	13.4
Canned crushed tomatoes (after sterilisation)	4	0.11	7.8

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

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

Tomatoes (glass house production)	0.2 mg/kg
Tomatoes (outdoor production)	0.1 mg/kg

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

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	13.7 % AR after 49 days (n = 1) 10.3 % AR after 56 days (n = 1) 2.7 % AR after 91 days (n = 1) 79.5 % AR after 59 days (n = 1)
Non-extractable residues after 100 days ‡	71.8 % AR after 28 days; 71.1 % AR after 49 days (n = 1) 75.5 % AR after 56 days (n = 1) 43.5 % AR after 3 days; 37.4 %AR after 91 days (n =1) 13.4 % AR after 14 days; 9.2 % AR after 59 days (n=1)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	No major metabolites (based on cold extracts) Max. metabolite formation rates (cold + harsh extracts): 3-Formamidophenyl methylcarbamate: 20.2 %AR 3-Aminophenyl methylcarbamate: 50.6 %AR 3-hydroxyformanilide: 17.6%AR

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

Anaerobic degradation ‡	Mineralisation: 2.9 - 5.9 % AR after 60 days (n = 2) Non-extractable residues: 62.3 - 64.5 % AR after 60 days (n = 2) Metabolites: N'-(3-hydroxyphenyl)-N'N-dimethylformamidine max. 8.8 % AR at day 7 3-Formamidophenyl methylcarbamate max. 12.0 % AR at day 7 3'-Hydroxyformanilide max. 9.8 % AR at day 8 3-Aminophenyl methylcarbamate max. 9.3 % AR at day 14
Soil photolysis ‡	Mineralisation: 4.2 % AR after 91.7 hours (n = 1) Non-extractable residues: 27.7 % AR after 91.7 hours (n = 1) Metabolites: N'-(3-hydroxyphenyl)-N'N-dimethylformamidine max. 22.9 % AR at 27.9 hours

‡ Endpoints identified by 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)

Method of calculation	Aerobic: 1st order kinetics (non-linear regression) Anaerobic: 1st order kinetics (non-linear regression)
Laboratory studies ‡ (range or median, with n value, with r^2 value)	All values normalised to 20°C &-10kPa soil moisture Formetanate: DT_{50lab} (20°C, aerobic): 5.97 – 12.75 days (n = 3) (r^2=0.987–0.995) Value appropriate for FOCUS modelling 12.75 days Metabolites N'-(3-hydroxyphenyl)-N'N-dimethylformamidine: DT_{50lab} (20°C, aerobic): 2.20 – 4.34 days (n = 2) (r^2=0.987–0.995) Value appropriate for FOCUS modelling 4.34 days 3-Formamidophenyl methylcarbamate: DT_{50lab} (20°C, aerobic): 0.92 – 1.15 days (n = 2) (r^2=0.987–0.995) Value appropriate for FOCUS modelling 1.15 days 3'-Hydroxyformanilide: DT_{50lab} (20°C, aerobic): 0.76 – 1.37 days (n = 2) 3-Aminophenyl methylcarbamate: DT_{50lab} (20°C, aerobic): 0.76 – 2.80 days (n = 2) (r^2=0.987–0.995) Value appropriate for FOCUS modelling 2.8 days Formetanate: DT_{90lab} (20°C, aerobic): 19.84 – 42.34 days (n = 3) (r^2=0.987–0.995) Formetanate: DT_{50lab} (10°C, aerobic): 13.1 – 28.1 days (n = 3) Formetanate: Kinetics: 1st order DT_{50lab} (Soil, 20°C, anaerobic): 5.9 – 7.6 days (n = 2)
	degradation in the saturated zone: no data submitted and no data required
Field studies ‡ (state location, range or median with n value)	California/USA: Graphically estimated DT values quoted are for all residues containing the 3-aminophenol moiety. DT_{50f}, orange trees, 1 x 5.16 kg a.s./ha: 6 - 10 days (n = 1) California/USA: DT_{50f}, alfalfa, 1.03 kg a.s./ha: 1 day (n = 1)
Soil accumulation and plateau concentration ‡	Not required.

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡	Formetanate: K_{fOC}: 140 – 620mL/g (1/n = 0.81 – 0.87; 4 soils) K_f: 1.49 – 3.00mL/g (4 soils) Metabolites: 3-Formamidophenyl methylcarbamate: K_{fOC}: 68 – 142mL/g (mean 107mL/g, 1/n = 0.864 – 0.915 mean 0.9; 4 soils) K_f: 0.69 – 3.15mL/g (mean 1.65mL/g, 4 soils) N'-(3-hydroxyphenyl)-N'N-dimethylformamidine: K_{fOC}: 368 – 1289mL/g(mean 801mL/g, 1/n = 0.829 – 0.904 mean 0.87; 4 soils) K_f: 1.79 – 40.2mL/g (mean 15.3mL/g, 4 soils) 3'-Hydroxyformanilide: K_{fOC}: 253 – 337mL/g (mean 298mL/g, 1/n = 0.850 – 0.906 mean 0.87; 4 soils) K_f: 1.59 – 9.3mL/g (mean 5.2mL/g, 4 soils) 3-Aminophenyl-N-methylcarbamate: K_{fOC}: 40 – 70mL/g (mean 57mL/g, 1/n = 0.66 – 0.88 mean 0.78; 3 soils) K_f: 0.761 – 2.32mL/g (mean 1.3, 3 soils)
pH dependence ‡ (yes / no) (if yes type of dependence)	Formetanate none observed but to avoid hydrolysis only a relatively narrow range of acid soils (pH 5.2-6.4) were tested. Based on pKa, lower adsorption at alkali soil pH may occur. Possible lower adsorption at higher pH would probably be compensated for by rapid (hydrolytic) degradation Metabolites: No Values selected as appropriate for FOCUS modelling. Formetanate: K_{fOC}: 140mL/g 1/n = 0.87 (lowest due to potential pH dependence). 3-Formamidophenyl methylcarbamate: K_{fOC}: 107mL/g, 1/n = 0.9 mean values N'-(3-hydroxyphenyl)-N'N-dimethylformamidine: K_{fOC}: 801mL/g, 1/n = 0.87 mean values 3'-Hydroxyformanilide: K_{fOC}: 298mL/g 1/n = 0.87 mean values 3-Aminophenyl-N-methylcarbamate: K_{fOC}: 57mL/g 1/n = 0.78 mean values

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

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

Column leaching ‡	Precipitation: 1050 mL within 5 days Leachate: 0.2 – 10.7 % AR in leachate (4 soils)
Aged residues leaching ‡	Sandy loam: Aged for 3 days Precipitation: 1L within 5 days Leachate: 0.2 – 1.1 % AR in leachate Sand: Aged for 31 days Precipitation: 230 mL per day (= 120 mm per day) Leachate: 4.9 – 5.1 % AR in leachate
Lysimeter/ field leaching studies ‡	Not required.

PEC (soil) (Annex IIIA, point 9.1.3)

Method of calculation	Parent; DT_{50}: 12.75 days N'-(3-hydroxyphenyl)-N'N-dimethylformamidine, DT_{50}: 4.34 days 3-Formamidophenyl methylcarbamate, DT_{50}: 1.15 days 3'-Hydroxyformanilide, DT_{50}: 1.37 days 3-Aminophenyl methylcarbamate, DT_{50}: 2.80 days Kinetics: 1st order

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

Application rate	Application rate: 0.5 kg a.s./ha PECs calculation for the degradation products was based on very unrealistic100 % metabolite formation rate. The application rate was corrected by the molecular weight ratio metabolite to parent. 0.32 kg N'-(3-hydroxyphenyl)-N'N-dimethylformamidine/ha 0.38 kg 3-Formamidophenyl methylcarbamate/ha 0.27 kg 3'-Hydroxyformanilide/ha 0.32 kg 3-Aminophenyl methylcarbamate/ha Crop: tomatoes and ornamental shrubbery Interception: 50 % Number of applications: 1

Parent

$PEC_{(s)}$ (mg/kg)	Tomatoes and Ornamental shrubbery (1 x 500 g a.s./ha, 50 % Interception)	
	Single application Actual	Single application Time weighted average
Initial	0.333	-
Short term 24h	0.316	0.324
2d	0.299	0.316
4d	0.268	0.300
Long term 7d	0.228	0.277
28d	0.073	0.171
50d	0.022	0.115
100d	0.001	0.061

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

Metabolites

PEC(s) (mg/kg) **N'-(3-hydroxyphenyl)-N'N-dimethylformamidine**	Tomatoes and Ornamental shrubbery (1 x 500 g a.s./ha, 50 % Interception)	
	Single application Actual	Single application Time weighted average
Initial	0.2133	-
Short term 24h	0.1818	0.1971
2d	0.1550	0.1826
4d	0.1126	0.1576
Long term 7d	0.0697	0.1284
28d	0.0024	0.0472
50d	0.0001	0.0267
100d	0.0000	0.0134

$PEC_{(s)}$ (mg/kg) **3-Formamidophenyl methylcarbamate**	Tomatoes and Ornamental shrubbery (1 x 500 g a.s./ha, 50 % Interception)	
	Single application Actual	Single application Time weighted average
Initial	0.2533	-
Short term 24h	0.1665	0.1889
2d	0.1300	0.1682
4d	0.0792	0.1354
Long term 7d	0.0377	0.1013
28d	0.0002	0.0307
50d	0.0000	0.0172
100d	0.0000	0.0086

PEC(s) (mg/kg) **3'-Hydroxyformanilide**	Tomatoes and Ornamental shrubbery (1 x 500 g a.s./ha, 50 % Interception)	
	Single application Actual	Single application Time weighted average
Initial	0.1800	-
Short term 24h	0.1085	0.1413
2d	0.0654	0.1132
4d	0.0238	0.0772

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

PEC(s) (mg/kg) **3'-Hydroxyformanilide**	Tomatoes and Ornamental shrubbery (1 x 500 g a.s./ha, 50 % Interception)	
	Single application Actual	Single application Time weighted average
Long term 7d	0.0052	0.0494
28d	0.0000	0.0127
50d	0.0000	0.0071
100d	0.0000	0.0036

$PEC_{(s)}$ (mg/kg) **3-Aminophenyl methylcarbamate**	Tomatoes and Ornamental shrubbery (1 x 500 g a.s./ha, 50 % Interception)	
	Single application Actual	Single application Time weighted average
Initial	0.2133	-
Short term 24h	0.1665	0.1889
2d	0.1300	0.1682
4d	0.0792	0.1354
Long term 7d	0.0377	0.1013
28d	0.0002	0.0307
50d	0.0000	0.0172
100d	0.0000	0.0086

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) ‡ (state pH and temperature)	pH 4 (20°C): DT_{50} 203 days pH 7 (20°C): DT_{50} 36 hours pH 9 (20°C): DT_{50} 2.84 hours Metabolites: N'-(3-hydroxyphenyl)-N'N-dimethylformamidine max. 19.6 % at pH 9 3-Formamidophenyl methylcarbamate max. 40.8 % at pH 7 3'-Hydroxyformanilide max. 31.1 % at pH 9 3-Aminophenyl methylcarbamate max. 1.4 % at pH 4

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

Photolytic degradation of active substance and relevant metabolites ‡	Xenon arc light, pH 5 and 7, 20°C: Degradation observed in the test solutions at each respective value was due to the hydrolysis of parent and not as a result of photolysis.
Readily biodegradable (yes/no)	Not according to OECD Guideline 301 B
Degradation in water/sediment	**Parent**
- DT_{50} water	0.2 d (pH 7.2) – 0.3 d (pH 6.5) FOCUS value 0.33d (longest due to indications of pH dependence)
- DT_{90} water	0.8 – 1.1 d
- DT_{50} sediment	0.3 d (pH 7.2) – 0.6 d (pH 6.5) FOCUS value 0.6d (longest due to indications of pH dependence)
- DT_{90} sediment	1.1– 2.0 d
- DT_{50} whole system	0.3 d (pH 7.2) – 0.4 d (pH 6.5)
- DT_{90} whole system	0.8 – 1.4 d
	3-Formamidophenyl methylcarbamate
- DT_{50} water	1.1– 2.2 d mean FOCUS value 1.65d
- DT_{90} water	3.7 – 7.2 d
- DT_{50} sediment	0.1– 4.6 d mean FOCUS value 2.37d
- DT_{90} sediment	0.5 – 15.2 d
- DT50 whole system	1.3 – 2.1 d
- DT90 whole system	4.2 - 6.9 d
	N'-(3-hydroxyphenyl)-N'N-dimethylformamidine
- DT_{50} water	0.3 – 0.4 d mean FOCUS value 0.33d
- DT_{90} water	0.9 – 1.4 d
- DT_{50} sediment	0.8 – 5.2 d mean FOCUS value 2.99d
- DT_{90} sediment	2.6 – 17.2 d
- DT_{50} whole system	0.3 – 0.5 d
- DT_{90} whole system	1.0 – 1.6 d
	3'-Hydroxyformanilide
- DT_{50} water	8.4 – 9.3 d mean FOCUS value 8.83d
- DT_{90} water	27.8 – 30.9 d
- DT_{50} sediment	5.6 – 17.0 d mean FOCUS value 11.32d
- DT_{90} sediment	18.7 - 56.4
- DT_{50} whole system	8.6 – 9.4 d
- DT_{90} whole system	28.6 – 31.4 d

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

	3-Aminophenyl methylcarbamate
- DT_{50} water	0.3 – 0.6 d mean FOCUS value 0.46d
- DT_{90} water	1.0 – 2.1 d
- DT_{50} sediment	0.1– 6.5 d mean FOCUS value 3.29d
- DT_{90} sediment	0.3 – 21.5 d
- DT_{50} whole system	0.5 – 0.8 d
- DT_{90} whole system	1.8 – 2.5 d
	3-Aminophenol
- DT_{50} water	0.1– 1.0 d mean FOCUS value 0.57d
- DT90 water	0.4 – 3.3 d
- DT_{50} sediment	0.4 – 8.6 d mean FOCUS value 4.49
- DT_{90} sediment	1.4 – 28.5 d
- DT_{50} whole system	0.3 – 1.2 d
- DT_{90} whole system	1.1 – 3.9 d
Mineralization	13.7 – 30.3 % AR after 28 – 70 d (n=2)
Non-extractable residues	52.7 – 58.2 % AR after 28 d (n=2)
Distribution in water / sediment systems (active substance) ‡	Parent: max. 6.7 – 16.6 % AR in sediment after 0.25 – 0.5 days.
Distribution in water / sediment systems (metabolites) ‡	**3-Aminophenol:** Surface water: Maximum of 22.9 % AR after 3 days. Sediment: Maximum of 5.5 % AR after 14 days. **3-Hydroxyformanilide:** Surface water: Maximum of 39.2 % AR after 7 days. Sediment: Maximum of 6.4 % AR after 3 days. **N'-(3-hydroxyphenyl)-N'N-dimethylformamidine** Surface water: Maximum of 11.6 % AR after 0.5 days. Sediment: Maximum of 4.4 % AR after 1 days. **3-Aminophenyl methylcarbamate:** Surface water: Maximum of 13.5 % AR after 3 days. Sediment: Maximum of 3.3 % AR after 3 days. **3-Formamidophenyl methylcarbamate:** Surface water: Maximum of 34.3 % AR after 0.5 days. Sediment: Maximum of 4.6 % AR after 3 days.

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

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

Formetanate

Method of calculation	Stepwise approach based on recommendations given in SANCO/4802/2001-rev.2. by the FOCUS Surface Water Scenarios Working Group Step 3 DT_{50} in soil 9.20 d DT_{50} in water 0.33 d DT_{50} in sediment 0.60 d Koc 340.3 mL/g Date of application: emergence
Application rate	1 x 0.5 kg a.s./ha in tomatoes (vegetables fruiting) and ornamental shrubs (field beans). Step 4 calculation was conducted only for the application to tomatoes considered as worst case covering also the use in ornamental shrubs
Main routes of entry	drift, drainage, run-off

Step 3 scenarios:

PEC_{sw} (µg/L)	Step 3 scenarios: tomatoes (vegetables fruiting)							
	D6: Thiva, ditch		R2: Porto, stream		R3: Bologna, stream		R4: Roujan, stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
0d	3.168	-	2.852	-	9.624	-	12.979	-
1d	0.320	1.384	0.003	2.046	0.016	4.984	0.074	9.618
2d	0.012	0.744	2.441	1.025	0.002	2.502	0.005	4.823
4d	0.000	0.373	1.877	0.908	3.377	1.252	0.000	2.412
7d	0.000	0.213	0.000	0.657	0.000	0.935	0.000	1.378
14d	0.015	0.110	0.000	0.357	0.000	0.519	0.000	0.909
21d	0.000	0.075	0.000	0.249	0.000	0.346	0.465	0.691
28d	0.003	0.057	0.000	0.187	0.000	0.260	0.000	0.539
42d	0.000	0.038	0.000	0.127	0.002	0.191	0.000	0.368
50d	0.000	0.032	0.000	0.113	0.000	0.166	0.000	0.309
100d	0.000	0.016	0.000	0.061	0.000	0.084	0.000	0.155

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

PEC_{sw} (µg/L)	Step 3 scenarios: ornamentals (field beans)							
	D2: Brimston, stream		D2: Brimston, ditch		D3:Vredepeel, ditch		D4: Skousbo, pond	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
0d	2.183	-	2.631	-	2.620	-	0.106	-
1d	0.000	0.174	0.962	1.646	0.214	1.076	0.051	0.075
2d	0.000	0.093	0.333	1.133	0.007	0.571	0.025	0.056
4d	0.000	0.071	0.333	0.634	0.000	0.286	0.006	0.035
7d	0.000	0.067	0.000	0.366	0.000	0.164	0.001	0.021
14d	0.004	0.038	0.025	0.184	0.000	0.082	0.000	0.011
21d	0.004	0.025	0.007	0.130	0.000	0.055	0.000	0.007
28d	0.002	0.019	0.001	0.098	0.000	0.041	0.000	0.005
42d	0.000	0.015	0.000	0.065	0.000	0.027	0.000	0.004
50d	0.020	0.014	0.021	0.073	0.000	0.023	0.000	0.003
100d	0.000	0.008	0.000	0.037	0.000	0.011	0.000	0.001

PEC_{sw} (µg/L)	Step 3 scenarios: ornamentals (field beans)							
	D4: Skousbo, stream		D6: Thiva, ditch, early application		D6: Thiva, ditch, late application		R1: Weiherbach, pond	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
0d	2.138	-	2.585	-	2.643	-	0.106	-
1d	0.000	0.120	0.012	0.727	0.103	0.800	0.040	0.068
2d	0.000	0.060	0.001	0.365	0.004	0.417	0.016	0.047
4d	0.000	0.030	0.000	0.183	0.000	0.209	0.002	0.027
7d	0.000	0.017	0.000	0.104	0.000	0.119	0.000	0.017
14d	0.000	0.009	0.000	0.052	0.000	0.060	0.000	0.012
21d	0.000	0.006	0.000	0.035	0.000	0.040	0.000	0.008
28d	0.000	0.004	0.000	0.026	0.000	0.030	0.002	0.008
42d	0.000	0.003	0.000	0.017	0.000	0.020	0.000	0.007
50d	0.000	0.002	0.000	0.015	0.000	0.017	0.000	0.006
100d	0.000	0.001	0.000	0.007	0.000	0.008	0.000	0.003

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

PEC_{sw} (µg/L)	Step 3 scenarios: ornamentals (field beans)							
	R1: Weiherbach, stream		R2: Porto, stream		R3: Bologna, stream		R4: Roujan, stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
0d	2.571	-	2.396	-	4.684	-	10.568	-
1d	0.003	1.310	0.000	1.535	0.869	3.996	0.058	7.826
2d	0.000	0.656	0.000	0.769	0.008	2.105	0.004	3.924
4d	0.106	0.328	1.190	0.693	0.001	1.054	0.000	1.963
7d	0.001	0.266	0.000	0.496	0.000	0.602	0.000	1.122
14d	0.040	0.160	1.821	0.279	0.000	0.301	0.000	0.754
21d	0.000	0.113	0.000	0.195	0.000	0.235	0.000	0.503
28d	0.000	0.101	0.000	0.146	0.000	0.176	0.000	0.400
42d	0.000	0.074	0.000	0.098	0.000	0.127	0.000	0.279
50d	0.000	0.062	0.000	0.085	0.000	0.110	0.000	0.239
100d	0.000	0.032	0.000	0.044	0.000	0.055	0.000	0.120

Step 4 scenarios:

PEC_{sw} (µg/L)	Step 4 scenarios: tomatoes (vegetables fruiting),			
	D6: Thiva, ditch; 40 m no-spray zone		R2: Porto, stream 10 m no-spray zone	
	Actual	TWA	Actual	TWA
0d	0.122	-	2.852	-
1d	0.012	0.053	0.003	2.046
2d	0.000	0.028	2.441	1.025
4d	0.000	0.014	1.877	0.908
7d	0.000	0.011	0.000	0.657
14d	0.015	0.007	0.000	0.357
21d	0.000	0.007	0.000	0.240
28d	0.003	0.005	0.000	0.180
42d	0.000	0.004	0.000	0.127
50d	0.000	0.003	0.000	0.113
100d	0.000	0.002	0.000	0.059

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

PEC (sediment)

Formetanate

Method of calculation	Stepwise approach based on recommendations given in SANCO/4802/2001-rev.2. by the FOCUS Surface Water Scenarios Working Group
Application rate	1 x 0.5 kg a.s./ha in tomatoes (vegetables fruiting) and ornamental shrubs (field beans). Step 4 calculation was conducted only for the application to tomatoes considered as worst case covering also the use in ornamental shrubs
Main routes of entry	drift, drainage, run-off

Step 3 scenarios:

Crop	Scenario	Initial PEC_{sed} (µg/kg)
vegetables fruiting (tomatoes)	D6 (Thiva, ditch)	0.512
	R2 (Porto, stream)	1.595
	R3 (Bologna, stream)	2.188
	R4 (Roujan, stream)	4.187
field beans (ornamental shrubs)	D2 (Brimston, stream)	0.096
	D2 (Brimston, ditch)	0.669
	D3 (Vredepeel, ditch)	0.399
	D4 (Skousbo, pond)	0.036
	D4 (Skousbo, stream)	0.080
	D6 (Thiva, ditch, early application)	0.335
	D6 (Thiva, ditch, late application)	0.276
	R1 (Weiherbach, pond)	0.030
	R1 (Weiherbach, stream)	0.668
	R2 (Porto, stream)	1.279
	R3 (Bologna, stream)	1.783
	R4 (Roujan, stream)	3.426

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

Step 4 scenarios:

Crop	Scenario	Initial PEC_{sed} (µg/kg)
vegetables fruiting (tomatoes)	D6 (Thiva, ditch) 40 m no-spray zone	0.021
	R2 (Porto, stream) 10 m no-spray zone	1.595

Degradation products

Method of calculation:	Step 3, FOCUS surface water scenarios PECsw calculation was based on the very unrealistic100 % metabolite formation rate. For each metabolite a separate calculation was conducted and the parent application rate was corrected by the molecular weight ratio metabolite to parent.
Main input parameters:	**N'-(3-hydroxyphenyl)-N'N-dimethylformamidine:** 1 x 0.32 kg/ha DT_{50} in soil 4.34 d DT_{50} in water 0.33 d Koc 368 mL/g **3-Formamidophenyl methylcarbamate:** 1 x 0.38 kg/ha DT_{50} in soil 1.15 d DT_{50} in water 1.65 d Koc 68 mL/g **3'-Hydroxyformanilide:** 1 x 0.27 kg /ha DT_{50} in soil 1.37 d DT_{50} in water 8.83 d Koc 253 mL/g **3-Aminophenyl methylcarbamate:** 1 x 0.32 kg /ha DT_{50} in soil 2.80 d DT_{50} in water 0.46 d Koc 40 mL/g
Main routes of entry	drift, drainage, run-off

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

N'-(3-hydroxyphenyl)-N'N-dimethylformamidine

Crop	Scenario	Initial PECsw [µg/L]
vegetables fruiting (tomatoes)	D6 (Thiva, ditch)	0.237
	R2 (Porto, stream)	0.732
	R3 (Bologna, stream)	3.402
	R4 (Roujan, stream)	4.261
field beans (ornamental shrubs)	D2 (Brimston, stream)	0.039
	D2 (Brimston, stream)	0.195
	D3 (Vredepeel, ditch)	0.194
	D4 (Skousbo, pond)	0.008
	D4 (Skousbo, stream)	0.000
	D6 (Thiva, ditch, early appl.)	0.191
	D6 (Thiva, ditch, late appl.)	0.305
	R1 (Weiherbach, pond)	0.025
	R1 (Weiherbach, stream)	0.657
	R2 (Porto, stream)	0.734
	R3 (Bologna, stream)	1.357
	R4 (Roujan, stream)	4.324

3-Formamidophenyl methylcarbamate

Crop	Scenario	Initial PECsw [µg/L]
vegetables fruiting (tomatoes)	D6 (Thiva, ditch)	0.828
	R2 (Porto, stream)	1.030
	R3 (Bologna, stream)	1.943
	R4 (Roujan, stream)	1.490
field beans (ornamental shrubs)	D2 (Brimston, stream)	4.081
	D2 (Brimston, ditch)	6.362
	D3 (Vredepeel, ditch)	0.684
	D4 (Skousbo, pond)	0.028
	D4 (Skousbo, stream)	0.000
	D6 (Thiva, ditch, early appl.)	0.678
	D6 (Thiva, ditch, late appl.)	1.815
	R1 (Weiherbach, pond)	0.028
	R1 (Weiherbach, stream)	0.248

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

Crop	Scenario	Initial PECsw [µg/L]
	R2 (Porto, stream)	1.190
	R3 (Bologna, stream)	0.063
	R4 (Roujan, stream)	1.442

3'-Hydroxyformanilide, may also be used as a worst case surrogate for 3'-aminophenol

Crop	Scenario	Initial PECsw [µg/L]
vegetables fruiting (tomatoes)	D6 (Thiva, ditch)	0.555
	R2 (Porto, stream)	0.276
	R3 (Bologna, stream)	0.963
	R4 (Roujan, stream)	0.907
field beans (ornamental shrubs)	D2 (Brimston, steram)	0.462
	D2 (Brimston, steram)	0.039
	D3 (Vredepeel, ditch)	0.460
	D4 (Skousbo, pond)	0.022
	D4 (Skousbo, stream)	0.000
	D6 (Thiva, ditch, early appl.)	0.000
	D6 (Thiva, ditch, late appl.)	0.000
	R1 (Weiherbach, pond)	0.022
	R1 (Weiherbach, stream)	0.120
	R2 (Porto, stream)	0.229
	R3 (Bologna, stream)	0.069
	R4 (Roujan, stream)	0.955

3-Aminophenyl methylcarbamate

Crop	Scenario	Initial PECsw [µg/L]
vegetables fruiting (tomatoes)	D6 (Thiva, ditch)	0.762
	R2 (Porto, stream)	1.889
	R3 (Bologna, stream)	5.777
	R4 (Roujan, stream)	5.899
field beans (ornamental shrubs)	D2 (Brimston, stream)	15.212
	D2 (Brimston, stream)	23.731
	D3 (Vredepeel, ditch)	0.227
	D4 (Skousbo, pond)	0.009

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

Crop	Scenario	Initial PECsw [µg/L]
	D4 (Skousbo, stream)	0.000
	D6 (Thiva, ditch, early appl.)	0.233
	D6 (Thiva, ditch, late appl.)	0.752
	R1 (Weiherbach, pond)	0.009
	R1 (Weiherbach, stream)	0.922
	R2 (Porto, stream)	2.169
	R3 (Bologna, stream)	0.701
	R4 (Roujan, stream)	5.521

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Model FOCUS PELMO 3.3.2 (Pesticide leaching model) Principal input parameter: Parent: Molecular weight 257.8 g/mol Solubility in water 822 g/L H $5*10^{-10}$ Pa x m^3 x mol^{-1} Koc: 171 mL/g (24 hour equilibrium value, at pH 5.2) 1/n=0.9 (default). DT_{50}: 12.75 days (worst-case) Plant interception 50% Degradation products: PECgw calculation was based on very unrealistic100 % metabolite formation rate. For each metabolite a separate PELMO calculation was conducted and the application rate was corrected by the molecular weight ratio metabolite to parent. All 1/n=0.9 (default) **N'-(3-hydroxyphenyl)-N'N-dimethylformamidine:** DT_{50} = 4.34 days (worst-case) Kfoc=368 mL/g **3-Formamidophenyl methylcarbamate:** DT_{50} = 1.15 days (worst-case) Kfoc= 68mL/g **3'-Hydroxyformanilide:** DT_{50} = 1.37 days (worst-case) Kfoc=253 mL/g **3-Aminophenyl methylcarbamate:** DT_{50} = 2.80 days (worst-case) Kfoc=40 mL/g

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

Application rates	1 x 0.5 kg a.s./ha 1 x 0.32 kg N'-(3-hydroxyphenyl)-N'N-dimethylformamidine/ha 1x 0.38 kg 3-Formamidophenyl methylcarbamate/ha 1 x 0.27 kg 3'-Hydroxyformanilide/ha 1 x 0.32 kg 3-Aminophenyl methylcarbamate/ha

$PEC_{(gw)}$

Maximum concentration	Not calculated by FOCUS shells, not required.
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Parent: < 0.001 µg/L N'-(3-hydroxyphenyl)-N'N-dimethylformamidine: < 0.001 µg/L 3-Formamidophenyl methylcarbamate: < 0.001 µg/L 3'-Hydroxyformanilide: < 0.001 µg/L 3-Aminophenyl methylcarbamate: < 0.001 µg/L

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

Direct photolysis in air ‡	Not studied – no data requested, not required
Quantum yield of direct phototransformation	Degradation observed in the test solutions at each respective pH value was due to the hydrolysis of the parent and not as a result of photolysis. Therefore, no quantum yield was calculated.
Photochemical oxidative degradation in air ‡	DT_{50} of 1.397 hours derived by the Atkinson method of calculation
Volatilization ‡	Not studied – no data requested, not required.

PEC (air)

Method of calculation	The parent is only slightly volatile (vapour pressure = 1.6×10^{-6} Pa). Thus it is concluded that it is unlikely that significant residues will occur in the air. Moreover, its reactivity with OH radicals in the troposphere is predicted to be rapid so long range transport is not expected.

$PEC_{(a)}$

Maximum concentration	Negligible

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

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	**For risk assessment** **Soil:** formetanate, 3-Formamidophenyl methylcarbamate, 3-Aminophenyl methylcarbamate, N'-(3-hydroxyphenyl)-N'N-dimethylformamidine, 3-hydroxyformanilide **Groundwater:** formetanate, 3-Formamidophenyl methylcarbamate, 3-Aminophenyl methylcarbamate, N'-(3-hydroxyphenyl)-N'N-dimethylformamidine, 3-hydroxyformanilide **Surface water:** formetanate, 3-Formamidophenyl methylcarbamate, 3-Aminophenyl methylcarbamate, N'-(3-hydroxyphenyl)-N'N-dimethylformamidine, 3-hydroxyformanilide, 3-aminophenol. **Sediment**: formetanate **Air**: formetanate **For monitoring** Formetanate and its salts

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

Soil (indicate location and type of study)	No data concerning adverse effects to the environment of the active ingredient have been reported.
Surface water (indicate location and type of study)	No data have been reported.
Ground water (indicate location and type of study)	No data have been reported.
Air (indicate location and type of study)	No data have been reported.

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Potential candidate for R53

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

Appendix 1.6: Effects on non-target Species

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

Acute toxicity to mammals ‡	LD_{50}: 21 mg Formetanate hydrochloride /kg bw (rats) (pooled data for males and females), 14.8 mg Formetanate hydrochloride /kg bw (females only)
Acute toxicity to birds ‡	LD_{50}: 11.5 mg Formetanate hydrochloride /kg bw (Mallard duck)
Acute toxicity to birds (study performed with an SP formulation containing 500 g/kg formetanate)	LD_{50}: 89 mg formulation/kg bw (Bobwhite quail) (corresponding to 52.2 mg a.s. Formetanate hydrochloride /kg bw)
Dietary toxicity to birds ‡	NOEC[1)]: 100 mg/kg diet (Mallard duck; corresponding to 22.7 mg Formetanate hydrochloride/kg bw/d) LC_{50}: 2086 mg/kg diet (Mallard duck) (corresponding to 116 mg Formetanate hydrochloride/kg bw/d)
Reproductive toxicity to birds ‡	NOEC: 160 mg/kg diet (Bobwhite quail, Mallard duck) (15.6 mg Formetanate hydrochloride/kg bw/d (Bobwhite quail)
Reproductive toxicity to mammals (ecotoxicological relevant endpoint)	NOEL: 250 ppm (rats) (corresponding to 22.4 mg Formetanate hydrochloride/kg bw/d)

1) $NOEC_{DD}$ to be used for Tier 1 risk assessment calculation due to occurrence of food avoidance in the study. Higher Tier TER calculations refer to the LC_{50DD} of 116 mg/kg bw/d derived from probit analysis of daily doses.

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.5	Tomatoes/ Ornamental shrubs	Medium herbivorous bird	acute	0.3 [1)]	10
0.5	Tomatoes/ Ornamental shrubs	Medium herbivorous bird	short-term	1.5 [2)]	10
0.5	Tomatoes/ Ornamental shrubs	Medium herbivorous bird	long-term	1.9	5

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.5	Tomatoes/ Ornamental shrubs	Medium herbivorous mammals	acute	1.2 [3)]	10
0.5	Tomatoes/ Ornamental shrubs	Medium herbivorous mammals	long-term	7.6	5
0.5	Tomatoes/ Ornamental shrubs	insectivorous bird	acute	0.4 [1)]	10
0.5	Tomatoes/ Ornamental shrubs	insectivorous bird	short-term	1.5 [2)]	10
0.5	Tomatoes/ Ornamental shrubs	insectivorous bird	long-term	1.0	5
0.5	Tomatoes/ Ornamental shrubs	insectivorous mammal	acute	3.4 [3)]	10
0.5	Tomatoes/ Ornamental shrubs	Insectivorous mammal	long-term	14.0	5

1) Based on LD_{50} from acute oral gavage study with mallard duck
2) Based on $NOEC_{DD}$ from 5-day dietary study with mallard duck
3) Based on LD_{50} for females only
4) A non peer reviewed refined assessment is available in addendum 2 of the DAR

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Laboratory tests ‡				
Oncorhynchus mykiss	SP Formulation with 500 g/kg Formetanate	acute, 96 h	LC_{50}	4.3
Lepomis macrochirus	Formetanate hydrochloride	acute, 96 h	LC_{50}	2.76
Pimephales promelas	Formetanate hydrochloride	early life stage, 32 d	NOEC	0.48

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Daphnia magna	Formetanate hydrochloride	acute, 48 h	EC_{50}	0.0017
Daphnia magna	Formetanate hydrochloride	chronic, 21 d	NOEC	0.0011
Daphnia longispina	Formetanate hydrochloride	acute, 48 h	EC_{50} NOEC	0.013 0.04
Simocephalus vetulus	Formetanate hydrochloride	acute, 48 h	EC_{50} NOEC	0.088 0.02
Thamnocephalus platyurus	Formetanate hydrochloride	acute, 48 h	EC_{50} NOEC	3.2 0.70
Gammarus spec.	Formetanate hydrochloride	acute, 48 h	EC_{50} NOEC	0.39 0.16
Brachionus calyciflorus	Formetanate hydrochloride	acute, 24 h	EC_{50} NOEC	1.9 0.44
Chaoborus spec.	Formetanate hydrochloride	acute, 48 h	EC_{50} NOEC	12 4.81
Cloeon spec.	Formetanate hydrochloride	acute, 48 h	EC_{50} NOEC	0.82 0.35
Chironomus riparius	Formetanate hydrochloride	acute, 48 h	EC_{50} NOEC	3.3 1.9
Lymnea stagnalis	Formetanate hydrochloride	acute, 48 h	EC_{50} NOEC	20.5 2.75
Selenastrum capricornutum	Formetanate hydrochloride	acute, 72 h	EbC50	1.3
Selenastrum capricornutum	SP Formulation with 500 g/kg Formetanate	acute, 72 h	EbC50	1.2
Brachydanio rerio	N'-(3-hydroxyphenyl)-N'N-dimethyl-formamidine	acute, 96 h	LC_{50}	> 1000
Microcosm or mesocosm tests				
Microcosm	SP Formulation with 500 g/kg Formetanate	56 days	NOEAEC	0.703

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

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
acute						
0.5	Tomatoes	*Lepomis macrochirus*	96 h	1.5	213	100
0.5	Tomatoes	*Daphnia magna*	48 h	1.5	0.1	100
0.5	Tomatoes	*Selenastrum capricornutum*	72 h	1.5	92	10
chronic						
0.5	Tomatoes	*Pimephales promelas*	32 d	1.5	37(1) / 891(2)	10
0.5	Tomatoes	*Daphnia magna*	21 d	1.5	0.08(1) / 1.6 (2)	10
higher-tier						
0.5	Tomatoes	Microcosm	56 d	1.5	54	not specified

1)TER_ibased on initial PEC-value; 2) TER based on time weighted average PEC-value.

Bioconcentration

Bioconcentration factor (BCF) ‡	< 1
Annex VI Trigger:for the bioconcentration factor	not applicable
Clearance time (CT_{50}) (CT_{90})	not applicable
Level of residues (%) in organisms after the 14 day depuration phase	not applicable

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

Acute oral toxicity ‡	LD_{50} = 0.16 µg Formetanate hydrochloride /bee
Acute contact toxicity ‡	LD_{50} = 1.02 µg Formetanate hydrochloride /bee

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

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.5	Tomatoes	oral	490	50
0.5	Tomatoes	contact	3125	50

Field or semi-field tests
Bees were exposed to residues, which were applied 1, 7 and 14 days before exposure at a rate of 500 g a.s./ha to flowering *Phacelia*. A slight increase in mortality was observed 7 days after application and no increase in mortality was evident in the treatment group of 14 days aged residues.

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

Laboratory tests

Species	Stage	Test Substance	Endpoint		HQ		Annex VI Trigger
			LR50 (g) Formetanate hydrochloride /ha)	Sublethal effects*	In field	Off field	
Typhlodromus pyri Predatory mite	Adult	SP Formulation with 500 g/kg Formetanate	0.78	No significant effects	638	17.7** 51***	2
Aphidius rhopalosiphi parasitoid	Adult	SP Formulation with 500 g/kg Formetanate	0.21	No significant effects	2381	66** 190***	2

* adverse effects as compared to the controls. Reproduction was assessed in treatment groups displaying mortality < 50%.
** based on drift value of 2.77 % for vegetables and ornamentals <50 cm with a spray distance of 1 m
*** based on drift value of 8.02 % for vegetables and ornamentals >50 cm with a spray distance of 3 m

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

Extended laboratory tests

Test species	Test system	Recommended application rate and drift rates[1] [g a.s./ha]	Application rate [g a.s./ha]	Endpoint		Annex VI Trigger
				Mortality	Sublethal effects	
Aphidius rhopalosiphi Parasitoid	Extended lab. test	500 205* 70**	0.5 - 5.0	96.7 % at 5.0 g formetanate hydrochloride/ha (LR_{50}=0.93 g Formetanate hydrochloride /ha)	No sig.effects up to 0.9 g Formetanate hydrochloride /ha	50 %
Aphidius rhopalosiphi Parasitoid	Aged residue test	500 205* 31***	35 210 500	10 % after 7 days at 35 g Formetanate hydrochloride /ha 43 % after 14 days at 210 g Formetanate hydrochloride /ha 20 % after 35 days at 500 g Formetanate hydrochloride /ha	No relevant effects up to 500 g Formetanate hydrochloride /ha	50 %
Chrysoperla carnea predator	Extended lab. test	500 20.5* 7**	6.25 - 100	47.8 % at 50 g Formetanate hydrochloride/ha (LR_{50}=64.0 g Formetanate hydrochloride /ha)	No sig.effects up to 50 g Formetanate hydrochloride /ha	50 %
Coccinella septempunctata predator	Extended lab. test	500 20.5* 7**	250 - 1000	0 % at 1000 g Formetanate hydrochloride /ha (LR_{50} >1000 g Formetanate hydrochloride /ha)	No sig.effects up to 1000 g Formetanate hydrochloride /ha	50 %

[1] drift rates based on the % drift value / vegetation distribution factor x safety factor (vegetation distribution factor = 1 for *A. rhopalosiphi* studies and = 10 for *C. carnea* and *C. septempunctata* studies)

* based on drift value of 8.02 % for vegetables and ornamentals >50 cm with a spray distance of 3 m

** based on drift value of 2.77 % for vegetables and ornamentals <50 cm with a spray distance of 1 m

*** based on drift value of 1.23 % for vegetables and ornamentals >50 cm with a spray distance of 10 m

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

Field or semi-field tests Due to the low and short-lasting effects seen in the extended laboratory tests demonstrating the acceptability of the intended uses for off-field and in-field scenarios, field-trials are considered not required.

Effects on earthworms (Annex IIA, point 8.4, Annex IIIA, point 10.6)

Acute toxicity ‡	LC_{50}: 1047.95 mg Formetanate hydrochloride /kg dry soil
Reproductive toxicity ‡	NOEC = 1.8 mg Formetanate hydrochloride /kg dry soil

Toxicity/exposure ratios for earthworms (Annex IIIA, point 10.6)

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
0.5	Tomatoes	acute	3147	10
0.5	Tomatoes	long term	5.41	5

Effects on soil micro-organisms (Annex IIA, point 8.5, Annex IIIA, point 10.7)

Nitrogen mineralization ‡	< 25 % (28 days) at both test concentrations (0.5 kg a.s./ha and 2.5 kg a.s./ha)
Carbon mineralization ‡	< 25 % (28 days) at both test concentrations (0.5 kg a.s./ha and 2.5 kg a.s./ha)

Effects on other non-target organisms believed to be at risk (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Vegetative vigour test	No effects at least up to 0.5 kg a.s./ha

Effects on biological methods for sewage treatments (Annex IIA, point 8.7)

Respiration inhibition test	No effects at least up to 1000 mg a.s./L

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N : Dangerous to the environment; R50: Very toxic to aquatic organisms;

‡ 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