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

methomyl

finalised: 23 June 2006

(revision of 21 July 2006 with minor editorial changes marked yellow)

SUMMARY

Methomyl 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.

United Kingdom being the designated rapporteur Member State submitted the DAR on methomyl in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 3 May 2004. Following a quality check on the DAR, the peer review was initiated on 28 June 2004 by dispatching the DAR for consultation of the Member States and the main applicant DuPont de Nemours. Makhteshim Agan ICC also submitted a dossier which the rapporteur Member State considered to be substantially incomplete. 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 September 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 7 June 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 insecticide comprise foliar spraying to control biting and sucking insects in cucumber, courgette, tomato and eggplants. Only the use as insecticide was evaluated. It should be noted that the use in grape was withdrawn during the EU peer review process.
The representative formulated product for the evaluation was "Methomyl 20 SL", a soluble concentrate (SL), registered in some Member States of the EU.

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

Adequate methods are available to monitor all compounds given in the respective residue definition. 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.

Methomyl is highly toxic via the oral, ocular and inhalation routes of exposure, but it has a low toxicity via the dermal route. On the basis of the data package available the proposed classification is T+, R26 'Very toxic by inhalation' and R25 'Toxic if swallowed'. It is not an eye or skin irritant and does not cause skin sensitisation. The overall short term NOAEL is approximately 10 mg/kg bw/day. Reliable data on effects on cholinesterase activity were not always determined. Based on the available studies, the weight of the evidence indicates that methomyl does not pose a genotoxic, reproductive or developmental concern. There was no evidence of methomyl-induced carcinogenic activity in rats or mice. The NOAEL for acute neurotoxicity is 0.25 mg/kg bw. The ADI, AOEL and ARfD were set at 0.0025 mg/kg bw, based on the acute neurotoxicity NOAEL applying a SF of 100.
The operator, worker and bystander risk assessment should be regarded as inconclusive, since the rapporteur Member State recalculated operator, worker and bystander exposure with dermal absorption values slightly different from the ones agreed during the experts' meeting; however, the assessment is not expected to change significantly even with the use of values agreed during the experts' meeting. The operator exposure estimates exceed the AOEL in all scenarios considered.

The metabolism of methomyl in fruits is fully elucidated. Four metabolic pathways were identified generally leading to metabolites of no toxicological concern, as formed as a result of hydrolysis of the carbamate ester link and further degradation. However at least 2 metabolites were identified with intact carbamate structure (IN-HUZ57 and IN-G6520) and are considered as toxicologically relevant. In fruits, these metabolites are present at much lower levels than the parent compound and their contribution to the global toxicological burden is expected to be minor. Therefore, only the parent compound is proposed to be included in the residue definition for monitoring and risk assessment in fruit crops. For other commodities dealt with at member state level, the need for inclusion of these metabolites in the residue definition for risk assessment should be carefully considered as it appears that their ratio to the parent compound may be significant on leafy parts of plants, based on information obtained on grape foliage.
A sufficient amount of supervised residue trials were conducted in accordance with the supported representative uses, demonstrating that a MRL of 0.5 mg/kg would be needed for table and wine grapes, while residues in fruiting vegetables are consistently below the Limit Of Quantification (0.02 mg/kg) of the analysis method. In processed commodities (grape juice and wine), residues are lower than in raw grapes, this resulting from a preferential transfer to solid fractions during processing and from a partial degradation of methomyl to methomyl oxime. This degradation product has however no toxicological relevance.

On the basis of the supported representative uses dealt with under this peer review, no livestock exposure to methomyl residues is expected. Due to the low persistency of methomyl in soil, no residue of methomyl is expected in following crops.
Acute and chronic exposure assessments to methomyl residues were performed. A potential acute risk was identified for all considered population subgroups resulting from the consumption of treated table grapes.

Degradation of methomyl under dark aerobic conditions in soil does not produce any major metabolite. Taking into consideration also studies performed with thiodicarb (where methomyl appears as metabolite) methomyl is low or moderate persistent in soil under aerobic conditions. Unextractable residues accounted for up to 32.2 % AR after 30 d and CO_2 for 75.4 % AR after 92 d. No new soil metabolites were identified in the soil photolysis study. Acetonitrile was detected as the major volatile metabolite. The meeting of MS experts considered that the potential environmental contamination by acetonitrile derived from the use of methomyl will be insignificant with respect to other anthropogenic sources. Under normal environmental conditions microbial degradation in soil is likely to predominate over the photolytic one.
In the available field studies for thiodicarb, field degradation half lives of thiodicarb and methomyl were longer than the ones measured under laboratory conditions. The rapporteur Member State normalized the field dissipation rates for methomyl using the average soil temperatures over the period resulting in corrected half lives in the range of those observed in laboratory studies.
Since the half life originally used to calculate PEC in soil was derived from a study finally not considered adequate, new PEC soil were calculated and reported in an addendum. Worst case laboratory half life of 15.2 d was used. Two applications of 450 g/ha with an interval of 14 d were calculated as a worst case representative use. Interception of 60 % (corresponding to leaf development BBCH 50) was assumed for vines and 70 % (corresponding to BBCH 20 onwards for tomatoes) was assumed for vegetables. However, the proposed representative uses do not restrict the application to any particular growing stage. Therefore, EFSA calculated peak PEC soil for tomatoes considering leaf development stages (growing stages BBCH 10-19; 50 % interception) in the updated addendum.
Methomyl is very high mobile in soil. A column (3 soils) and an aged column (1 soil) leaching studies are available for methomyl. In the column leaching study methomyl in leachate represented 6.6 – 55 % AR. Methomyl oxime was observed up to 2.2 % AR in soil and 1.7 % AR in leachate. In the aged column study, the major radioactive component in the leachate (5 % AR) co-chromatographed with methomyl.
Neither hydrolysis nor photolysis are expected to contribute significantly to the degradation of methomyl in the aqueous environment. Methomyl is not ready biodegradable.
In water / sediment systems, methomyl partitions to the sediment to levels up to 11.4 % AR after one day. Degradation occurred with half lives between 2.5 to 4.8 days in the whole systems. Dissipation from the water phase was between 3.5 and 4.5 d. Unextractable residues in the sediment reached a maximum of 20.1 % AR after 14 d declining to 14.7 % AR at the end of the study (102 d). CO_2 reached a maximum of 32.1 – 72.3 % AR at the end of the studies. Acetonitrile appears as a major

metabolite in some systems both in the sediment and as volatile metabolite. The meeting of MS experts considered that the potential environmental contamination by acetonitrile derived from the use of methomyl will be insignificant with respect to other anthropogenic sources.

$PEC_{SW\ /\ SED}$ values for parent methomyl were calculated based only in spray drift loadings and considering two categories. The first category is 'late grapes and listed tall vegetables' (i.e. tomatoes and grapes post-flowering) and the second category is 'listed low vegetables' (i.e. courgettes and aubergines). For cucumber it is necessary for Member States to consider which category cucumbers fit into under their growing regimes. The values were recalculated for a water phase half life of 4.5 d in the addendum.

The potential of ground water contamination by methomyl and its minor soil metabolite methomyl oxime was simulated by the applicant and recalculated by the rapporteur Member State for the representative uses in vines and tomatoes with FOCUS PRZM 2.2.1 and FOCUS PEARL 1.1.1 models for all relevant scenarios. None of the crop / scenario combination exceeded the 0.1 µg / L on the 80^{th} percentile annual average concentrations neither for methomyl nor for methomyl oxime.

Concentration of methomyl in the air compartment and transport through it is not expected to be significant.

Methomyl is intended to be used in cucumber/courgette, tomato/eggplant and grape (table & wine). The use in grapes is not longer supported by the applicant for the EU review process (i.e. with respect to Annex I inclusion). Nevertheless the risk from this originally intended use is reported in the section on ecotoxicology as far as the risk assessment is available.

Based on the assessment according to EPPO (1992) the short and long term risk to birds can be regarded as low. The first tier acute risk to insectivorous birds is considered to be high. The applicant should be asked to address the acute risk from methomyl on the same basis as was done by the PPR Panel for pirimicarb. Furthermore the applicant is requested to provide a first tier risk assessment based on SANCO/4145/2000 and the dietary and reproduction endpoints for birds in terms of mg a.s./kg bw/day and a revised risk assessment. Based on the assessment according to EPPO (1992) both the acute and the long term risk to herbivorous mammals in grapes have to be regarded as high. Based on a weight of evidence approach, this long term risk was considered to be addressed. The acute risk from methomyl should be refined by the applicant on the same basis as was done by the PPR Panel for pirimicarb. A low risk to insectivorous mammals was identified in cucumber/courgette and tomato/eggplant if calculated according to EPPO (1992).

The EFSA recalculated the first tier risk to birds and mammals according to SANCO/4145/2000. Based on this risk assessment the short term risk to birds can be regarded as low but a high acute and long term risk was identified as well as a high acute and long term risk to mammals for all representative uses evaluated. Therefore the applicant is requested to submit a refinement of the long term risk to birds and mammals if the risk is assessed according to the latest guidance document (SANCO/4145/2000). For the acute risk to birds and mammals see outstanding data gap discussed above. A risk for birds and mammals from consumption of contaminated drinking water was identified which the EFSA proposes to be addressed.

A high risk to aquatic organisms was identified for which risk mitigation measures such as a buffer zone of 50 metres for 'late grapes and listed tall vegetables' and a buffer zone of 30 metres for 'listed low vegetables' should be taken into account.
A high risk to bees was identified. Risk mitigation measures to avoid all contact with bees are considered necessary. No data to establish a withholding period is available.
A high risk to non-target arthropods was identified. The applicant is asked to refine the risk assessment for non-target arthropods for both the in-field and off-field areas. The risk can only be concluded once this data becomes available but risk mitigation measure will possibly be necessary.
The acute risk to earthworms is considered to be low. In addition also the long term risk to earthworms can be considered as low for the representative uses in cucumber/courgette and tomato/eggplant for growth stages from BBCH 20 onwards. A long term risk to earthworms in grapes and in fruiting vegetables before growth stage BBCH 20 was identified. It is proposed that the applicant should address this risk.
The risk to soil micro-organisms, other soil non-target macro-organisms, non-target plants and biological methods for sewage treatment is considered to be low.

Key words: methomyl, peer review, risk assessment, pesticide, 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. Methomyl is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating United Kingdom as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, United Kingdom submitted the report of its initial evaluation of the dossier on methomyl, hereafter referred to as the draft assessment report, to the EFSA on 3 May 2004. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the draft assessment report was distributed for consultation on 28 June 2004 to the Member States and the main applicant DuPont de Nemours as identified by the rapporteur Member State. Makhteshim Agan ICC also submitted a dossier which was found to be substantially incomplete. On this basis the rapporteur Member State has checked only the identity and impurities of methomyl in this latter, incomplete, dossier and taken into consideration the information available where this might indicate a greater risk than that identified by the data in the other dossier submitted.

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 September 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 7 June 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 09 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 19 June 2006)

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

Methomyl is the ISO common name for *S*-methyl (*EZ*)-*N*-(methylcarbamoyloxy)thioacetimidate (IUPAC). It should be noted that neither the ISO common name nor the IUPAC identify the configuration but the *Z*- or *cis*-isomer is so strongly favored thermodynamically that the *E*- or *trans*-isomer is not detectable in practice.

Methomyl belongs to the class of oxime carbamate insecticides such as aldicarb, oxamyl and thiodicarb. Methomyl is taken up via the cuticle (contact) or by ingestion and acts by inhibition of the enzyme acetylchlolinesterase.

The representative formulated product for the evaluation was "Methomyl 20 SL", a soluble concentrate (SL), registered in some Member States of the EU.

The evaluated representative uses as insecticide comprise foliar spraying to control biting and sucking insects in cucumber, courgette, tomato, and eggplants. Only the use as insecticide was evaluated. It should be noted that the use in grape was withdrawn during the EU peer review process.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of methomyl as manufactured should not be less than 985 g/kg, which is higher than the minimum purity given in the FAO specification 264/TC (2002) of 980 g/kg. The higher value relates to the submitted results of current batch analysis and not to any toxicological concern to increase the minimum purity.
The technical material contains no relevant impurities.

Whether or not the second source can be regarded as comparable was discussed by the rapporteur Member State in the supplement to Volume 4 (Report on the Makhteshim-Agan source; Draft June 2004). Due to the fact that additional data on impurities were required (revisions to the specification and supporting information on purity of process reagents), it was not possible to conclude on the comparability. However, the rapporteur Member State has since received the outstanding data and has prepared a revision 1 (July 2005) to the supplement, the rapporteur Member State did not distribute this report to the Commission, the Member States or the EFSA.

The content of methomyl in the representative formulation is 200 g/L (pure).

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 methomyl or the respective formulation.

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

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of methomyl 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. methomyl in food of plant origin, in soil, water and air. Also a method for the determination of residue (methomyl is converted into methomyl oxime[3]) in blood is available.

[3] methomyl oxime (IN-X1177): N-hydroxyethanimidothioic acid methyl ester

The methodology used is HPLC with post column derivatisation and fluorescence detection, HPLC with MS detection or GC-MS. 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 meeting of experts (EPCO 35, September 2005) on identity, physical and chemical properties and analytical methods was limited to some clarification with respect to the specification of the technical material and certain properties of the plant protection product.

2. Mammalian toxicology

Methomyl was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 33) in September 2005.

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

Methomyl was readily absorbed from the gastrointestinal tract and rapidly eliminated within 24 hours from dosing (80% in the rat and 63% in the monkey). Urinary excretion accounted for 53% of the administered dose in rats and 29% in monkeys. Expired air accounted for approximately 33% of the administered dose in rats and 39% in monkeys. No specific bioaccumulation was noted with the exception of some radioactivity in red blood cells. In rats the major urine metabolite is the mercapturic acid derivative.[4] Acetonitrile is the major residue in blood and liver. In the monkey, over 18 metabolites were observed, none of which were greater than 4% and included those metabolites common with the rat. The monkey excretes more $^{14}CO_2$ and less ^{14}C-acetonitrile than the rat in expired air, and excretes considerably less of the mercapturic acid derivative of methomyl in urine (0.8% in monkey, 18% in rat); the monkey excreted a greater number of urinary metabolites.

2.2. Acute toxicity

Methomyl is highly toxic via the oral (LD_{50} 30 mg/kg bw), ocular and inhalation (LC_{50} 0.215 mg/L) routes of exposure, but it has a low toxicity via the dermal route. On the basis of the data package available the proposed classification of methomyl is **T+, R26 'Very toxic by inhalation'** and **R25 'Toxic if swallowed'**. It is not an eye or skin irritant and does not cause skin sensitisation. The adequacy of the local lymph node assay reported in the DAR was discussed in the meeting. At the top dose, ~2500 mg/kg bw, all animals died. While no deaths occurred in rats after an acute dermal dose of 2000 mg/kg bw, evidence of ChE inhibition was noted. Therefore the mortality was considered to be treatment-related, possibly as a result of oral ingestion through grooming. It was noted that in the surviving animals no sensitisation response was observed. Therefore the study was considered adequate, and confirmed the absence of sensitisation potential.

[4] methomyl mercapturate: *N*-acetyl-*S*-[1-[[[(methylamino)carbonyl]oxy]imino]ethyl]-L-cysteine (CAS)

2.3. SHORT TERM TOXICITY

Short-term feeding studies have been conducted in rats, mice and dogs. The studies showed some drawbacks (not conducted to modern protocols or standards, many of them did not carry out ophthalmologic examinations or reliable determinations of brain cholinesterase activity). The meeting agreed on a relevant overall NOAEL of approximately 10 mg/kg bw/day from dietary studies in rats, dogs and mice.

2.4. GENOTOXICITY

Negative results were obtained in all the studies submitted (including an *in vivo* clastogenicity assay and a bone marrow micronucleus assay). Positive results have been reported in the literature (two reports); the company evaluated two published papers and submitted a summary of their findings. Based on deficiencies in the study protocols and the route of administration (i.p. injection) in the *in vivo* study, the company considered these publications not suitable for assessing the genotoxic potential of methomyl. An *in vitro* cytogenicity test was provided and was clearly negative. Based on the available studies, the weight of the evidence indicates that methomyl does not pose a genotoxic concern.

2.5. LONG TERM TOXICITY

In the long-term study in rats, body weight effects and haematological changes were observed (reduced RBC count, haemoglobin and haematocrit). In the long-term study in mice, reduced survival and transient haematological changes (as seen in rats) were observed. The experts agreed on a NOAEL of 3 mg/kg bw/day from the 2 year study in dog, based on liver and spleen histopathology records at higher doses. There was no evidence of methomyl-induced carcinogenic activity in rats or mice.

2.6. REPRODUCTIVE TOXICITY

In the two-generation reproduction toxicity study, the main effects on parental animals were reduced body weight and food consumption, and increased relative spleen weight. There were no effects on reproduction and fertility but the combined mean pup weights were reduced. In the three generation reproduction toxicity study, there were no effects on parents or reproduction and fertility. Pup weight and food consumption were reduced in F3 pups. The parental and offspring NOAEL was 4.6 mg/kg bw/day and the reproductive NOAEL 80 mg/kg bw/day.

Developmental toxicity studies were conducted in rats and rabbits. In the rat developmental study, the maternal effects included reduced body weight and food consumption. There were no effects on the rat foetuses. In the rabbit developmental study, deaths, decreased body weight and clinical signs of cholinesterase activity were observed in the dams. There was no evidence of methomyl-induced teratogenic activity in rats or rabbits. Maternal and developmental NOAELs were 6 mg/kg bw/day and 16 mg/kg bw/day, respectively.

2.7. NEUROTOXICITY

The NOAEL for acute neurotoxicity was 0.25 mg/kg bw based on reversible dose-related brain cholinesterase activity; methomyl did not show any evidence of delayed toxicity.

2.8. FURTHER STUDIES

Several additional studies were performed to assess the reversibility of cholinesterase inhibition in rats, acute oral administration in rats, repeated oral dosing in rats and the *in vitro* activity of human and rat cholinesterase. A human volunteer study was also carried out to evaluate cholinesterase activity and the potential clinical signs of systemic toxicity in humans.

The potential toxicity of the plant metabolite IN HUZ57[5], identified in the grape metabolism study, was discussed during the meeting. It was considered that it is still of potential toxicological concern (it has the carbamate moiety and insecticidal activity although lower than that of methomyl). In the absence of data however, it was considered to have a potential for higher toxicity than methomyl.

The plant metabolite IN G6520[6] retained the carbamate moiety and was potentially more toxic than methomyl. IN NR282[7] was not considered of toxicological concern due to the absence of the carbamate moiety.

Methomyl oxime (IN-X1177) toxicity was discussed in the DAR: they lose their biological activity upon cleavage of the carbamate moiety; therefore they are not expected to induce acetylcholinesterase inhibition as the carbamate moiety is absent.

2.9. Medical data

In a human volunteer study, a statistically significant decrease in RBC cholinesterase activity at doses of 0.2 and 0.3 mg/kg bw was registered within 1.75 hours post dosing; a single occurrence of a mild headache at a dose of 0.3 mg/kg bw and quantitatively increased salivation at 0.2 and 0.3 mg/kg bw were reported. Red blood cholinesterase activity was depressed by 19% at 0.1 mg/kg bw at 1.25 hour post dosing. Plasma cholinesterase activity was depressed at 0.2 mg/kg bw and above.

The meeting considered the limitations of the human study, including the small group sizes. The meeting additionally discussed the relative sensitivities of RBC and brain ChE in species investigated (equal sensitivity in the acute gavage neurotoxicity study, greater sensitivity in the brain in the rabbit dermal study), and the fact that the relative sensitivity in humans was not known. The data was not considered adequate for the derivation of human reference values.

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

ADI, AOEL, ARfD

The meeting considered that the NOAEL of 0.25 mg/kg bw from the rat acute neurotoxicity study was appropriate, with the use of a safety factor of 100 to derive an ARfD and AOEL of 0.0025 mg/kg

[5] Hydroxy-cysteine derivative of methomyl (IN HUZ57): 9-hydroxy-6-methyl-3-oxo-4-oxa-7-thia-2,5-diazadec-5-en-10-oic acid

[6] Hydroxy methyl methomyl (IN G6520): methyl *N*-[[[(hydroxymethyl)amino]carbonyl]oxy]ethanimidothioate

[7] IN NR282: 2-methyl-4-thiazolemethanol

bw. It was noted that it was not possible to set the ADI using a longer duration study as these had NOAELs of >0.25 mg/kg bw. Therefore the ADI was also set at 0.0025 mg/kg bw/day.

2.11. DERMAL ABSORPTION

The dermal absorption was established with an *in vivo* rat data and *in vitro* rat, human and rabbit skin study. The values proposed in the DAR were 10% and 1% for the dilution and concentrate, respectively. The meeting derived dermal absorption values of 12.5% for the dilution and 2.5% for the concentrate Methomyl 20SL by taking the total value in the skin at 66 hours and correcting for the rat:human peak flux value.

In the recently submitted addendum (March 2006) the rapporteur Member State reconsidered these values, which were based on the *in vivo* rat data but corrected by a rabbit:human peak flux data instead of rat:human peak flux data. The rapporteur Member State considered that the rabbit data should not be used to determine a correction factor to be applied on *in vivo* rat data. Therefore, the rapporteur Member State considered more appropriate that the rat *in vivo*/*in vitro* rat:human data should be used to determine the dermal penetration values, i.e. 14% for the aqueous dilution and 0.4% for the concentrate. This proposal was not peer reviewed by MSs.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

Operator exposure

(DAR assessment)

In the DAR, the operator exposure estimates have been assessed using the German model and UK POEM; the use of 'Methomyl 20SL' on fruiting vegetable crops through tractor-mounted/trailed equipment resulted in an estimated systemic exposure exceeding the AOEL of 0.005 mg/kg bw/day for all scenarios except for operators wearing protective gloves when handling the concentrate and coveralls and protective gloves during application in field crops.

Calculations based on operator monitoring (dosimetry) data indicate that the use of 'Methomyl 20SL' on grapes through tractor-mounted/trailed equipment result in an exposure level above the AOEL for an operator wearing protective equipment.

EPCO expert's meetings

According to the EPCO outcomes (dermal absorption values and AOEL), the rapporteur Member State was asked to recalculate the operator exposure. In the addendum submitted in March 2006, the rapporteur Member State refined calculations considering dermal absorption values different from the ones agreed during the meeting (see 2.11 for the explanation). The AOEL considered for the re-calculations was 0.0025 mg/kg bw/day, as agreed during the EPCO meeting.

EFSA notes that the rapporteur Member State did not perform recalculations with the dermal absorption values agreed during the experts' meeting; however, the assessment is not expected to change significantly even with the use of values agreed during the experts' meeting.

The recalculations are as follows:

Model	Method	% of the AOEL No PPE	% of the AOEL With PPE
German	Orchard sprayer Grapevines	3,370	524 *
	Field crop sprayer	1,526	112 *
	Knapsack sprayer	1,755	314 *
UK POEM	Orchard sprayer Grapevines	>11,000	> 8,100 §
	Field crop sprayer	4,166	610 °
	Knapsack sprayer (low crops)	>11,000	>1,900 ^

* Gloves when handling the concentrate, coveralls and gloves during application

§ Gloves when handling the concentrate and during application

° Gloves when handling the concentrate and contaminated surfaces

^ Gloves when handling the concentrate, impermeable coveralls and gloves during application

Worker exposure

(DAR assessment)

Worker exposure estimates based on dislodgeable foliar residue decline studies and using published transfer coefficient data indicate that the levels of systemic exposure to methomyl for an unprotected worker harvesting field crops and grapes treated with 'Methomyl 20SL' were likely to be within the AOEL of 0.005 mg/kg bw/day.

EPCO expert's meetings

Recalculations have been performed by the rapporteur Member State (dermal penetration values of 14% for the aqueous dilution and 0.4% for the concentrate), showing exposure value ranging from 40% to 81% of the AOEL (field crops and grapevines, respectively), considering the dermal absorption values proposed by the rapporteur Member State.

EFSA notes that the rapporteur Member State did not perform recalculations with the dermal absorption values agreed during the experts' meeting.

Bystander exposure

(DAR assessment)

Bystander exposure estimates based on published field study measurements indicated that the level of systemic exposure to methomyl for an unprotected bystander at the time of application was below the AOEL of 0.005 mg/kg bw/day for the use of 'Methomyl 20SL' on field crops but above for the use on grapes.

EPCO expert's meetings

Recalculations have been performed by the rapporteur Member State (dermal penetration values of 14% for the aqueous dilution and 0.4% for the concentrate), showing exposure value ranging from

12% to 406% of the AOEL (field crops and grapevines, respectively), considering the dermal absorption values proposed by the rapporteur Member State.

EFSA notes that the rapporteur Member State did not perform recalculations with the dermal abortion values agreed during the experts' meeting.

In conclusion, the operator, worker and bystander risk assessment should be regarded as inconclusive due to the lack of refined calculations according to the EPCO outcomes.

3. Residues

Methomyl was discussed at EPCO experts' meeting for residues (EPCO 34) in September 2005.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of methomyl has been investigated in grapes. The compound was applied as spray treatment and samples of grapes and leaves were collected 2, 7 and 14 days after application. At 14 days PHI, 88 and 68 % of the TRR in berries and foliage respectively were extractable. Four different metabolic pathways were identified. The primary pathway is supposed to involve the displacement of the S-methyl moiety by glutathione, which in turn is catabolised to its cysteine derivative, being further either hydroxylated to IN-HUZ57 or cleaved to the free thiol. The second pathway involves hydrolysis of the carbamate ester to methomyl oxime (IN-X1177). The third pathway involves oxidation on the methylamino substituent to form IN-G6520. The fourth pathway involves the isomeration of methomyl to its *E*-isomer followed by hydrolysis of the carbamate ester and formation of acetonitrile, which is further either volatilised, derived to IN-NR282 through a cysteine conjugation reaction or ultimately degraded to acetamide, acetic acid and carbon dioxide. Most of the compounds identified can be conjugated to glucose.

The metabolic pattern in fruits and leaves were rather different with methomyl being by far the major compound of the residue in fruits, while it was only a minor component of the residue in foliage samples. In foliage, IN-HUZ57, IN-G6520 and IN-NR282 were present in higher amounts than the parent compound. These metabolites are not present in the rat metabolism and the expert meeting on toxicology (refer to point 2.8) discussed their toxicological relevance. It was concluded that IN-HUZ57 and IN-G6520 should be considered at least as toxic as the parent compound as they still possess the carbamate moiety, while IN-NR282 could be considered as non relevant. The decision as to whether the 2 toxicologically relevant metabolites should or not be included in the residue definition for risk assessment was extensively discussed in the expert meeting. It was finally agreed to consider only methomyl in the residue definition for monitoring and risk assessment given that levels in fruits of IN-HUZ57 and IN-G6520 are one order of magnitude lower than that of methomyl, and their contribution to the global toxicological burden is therefore expected to be minor. Member States should however be aware that this definition is only applicable to the fruit group of commodities.

Further metabolism studies on tobacco, cabbage and maize were also submitted by the notifier, but these studies could not be used as they were not performed according to modern standards, were mainly translocation and uptake studies and gave no qualitative and quantitative information on the metabolic pathway. For crop groups other than fruits, Members States should require relevant and valid information to assess the ratio parent/toxicologically relevant metabolites to establish a residue definition for an adequate protection of consumer's health.

A sufficient number of supervised residue trials were submitted in accordance with the supported representative uses.

For grapevines, a total of 21 valid trials were conducted, 10 in Northern Europe and 11 in Southern Europe. The rapporteur Member State noted that there was no significant difference between both regions. The Highest Residue (HR) and Supervised Trials Median Residue (STMR) were respectively 0.59 and 0.09 mg/kg. For fruiting vegetables, a total of 18 acceptable trials were available (6 on cucumbers, 3 on courgettes and 9 on tomatoes). All these trials lead to residues below the Limit of Quantification (LOQ) of the method of analysis used (0.02 mg/kg). The validity of these results are supported by storage stability studies in grapes, processed grape fractions, broccoli, lettuce, potato, bean seed and peanut, demonstrating that the compound is stable under deep freeze condition for at least 24 months (for processed grape fractions the duration of the study was limited to 9 months, but no sign of degradation was present).

The effects of processing on the nature of the residues were investigated through hydrolysis studies simulating sterilisation, baking, boiling and pasteurisation. These studies showed that, although remaining the major compound present at the end of the simulated process, methomyl is degraded to an extent which depends on the severity of the pH and temperature conditions. The major degradation product was identified as methomyl oxime. This compound resulting from the hydrolysis of the carbamate ester link is less toxic than the parent compound and does not contribute to the inhibition of cholinesterase (refer to point 2.8). Therefore, no specific residue definition is needed for processed commodities. Processing studies were performed on grape samples taken from 4 residue trials to produce wine, grape juice and raisins. A mass balance study was conducted using the data of one trial, demonstrating a slightly preferential transfer to solid (pomace) fractions rather than to liquid fractions (juice and wine). Average transfer factors to grape juice and wine were calculated to be 0.21 and 0.58 respectively. Drying has a reducing effect on the residue level, with a low transfer factor to raisins (0.20 for a drying process of 5-7 days at 60°C). Similarly dry pomace contains generally less residues than wet pomace.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

No data were submitted to investigate the potential transfer of soil residues to following crops. The reason is the short residual nature of methomyl in soil (DT_{50} ranging from 4 to 8 days and longest DT_{90} value found to be 43 days). In addition to this, the metabolites formed in soil are of no toxicological concern (methomyl oxime being the major hydrolysis product with a DT_{50} of less than 1 day). No MRL or plant-back restriction is needed.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Given the representative uses supported by the notifier, no exposure of livestock to methomyl residues is expected. However, metabolism studies in lactating goats and laying hens were submitted. These studies indicated that methomyl is extensively metabolised in livestock. No residues of parent compound or structurally related metabolites were present in tissues. Acetonitrile, thiocyanate and acetamide were detected as ultimate degradation products, before incorporation of the administered radioactivity in natural molecular constituents or elimination through expired volatile compounds.
A residue definition for animal products and the establishment of MRLs for these commodities is not required or necessary.

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 National Estimated Daily Intakes (NEDI). Two consumption patterns were considered: the WHO European typical diet for adult consumers, the diets in UK for 10 population subgroups including infants, toddlers, children and adults, which take into consideration high individual consumption levels (at the 97.5th percentile of the distribution of consumptions in the respective populations).
A TMDI calculation was performed for the WHO diet. Methomyl residues were considered to be at the level of the HR found in supervised trials, and the consumer's body weight was 70 kg. In these conditions, the exposure was assessed to reach 6 % of the ADI.
A NEDI calculation was performed for the UK diet. Methomyl residues were considered to be at the level of the STMR found in supervised trials and a processing factor from grapes to wine of 0.58 was used. The highest exposures among the 10 population subgroups were determined for toddlers and vegetarians, reaching 20 % of the ADI.

Acute exposure.

The acute exposure to residues of methomyl in grapes and fruiting vegetables has been assessed according to the WHO model for conducting National Estimates of Short Term Intakes (NESTI) calculations. Large portion consumption data for 10 population subgroups (including infants, toddlers, children and adults) in UK were used. Calculations were carried out considering residues in composite samples of treated commodities at the level of the HR found in supervised trials (which is slightly higher than the proposed MRL) for grapes and at the level of the LOQ for fruiting vegetables. The variability factor used was 5 for grapes, aubergines and cucumbers and 7 for tomatoes and courgettes. Under these conditions the NESTI were found to be below the ARfD of methomyl for fruiting vegetables, but were largely in excess of the ARfD for table grapes: this exceedence was noted for all population subgroups, and the most critical NESTI value was found for toddlers with a potential acute exposure amounting to 1400 % of the ARfD. No exceedence of the ARfD was noted for wine as it can be considered that the unit to unit variability does not apply for wine production.

3.4. PROPOSED MRLS

Based on the results of supervised residue trials on grapes and their analysis according to statistical tools recommended by current guidelines a MRL of 0.5 mg/kg for methomyl should be set to accommodate the supported representative use. However, as mentioned in point 3.3, a risk for the consumer has been identified for table grapes.

For tomatoes, aubergines, cucumbers and courgettes the MRL is proposed to be set at the LOQ of the method of analysis (0.02 mg/kg).

4. Environmental fate and behaviour

Methomyl was discussed at the meeting of MS experts on fate and behaviour in the environment EPCO 31 on basis of the information presented in the DAR and Addendum 1 (August 2005). Some end points are derived from studies presented in the thiodicarb dossier. These studies were discussed in the meeting of MS experts EPCO 16.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation of methomyl in soil under dark aerobic conditions at 20 ºC or 25 ºC was investigated in two studies. A total of four soils were investigated covering a range of pH (5.1 – 7.8), clay content (6.0 % - 13.4 %) and organic carbon (0.54 % - 2.1 %). Degradation in one of the soils was also tested at 10 °C. No major metabolite was identified in these studies. Methomyl oxime (max 2.2 % AR after 1d) was identified as a minor soil metabolite. Unextractable residues accounted for up to 32.2 % AR after 30 d and CO_2 for 75.4 % AR after 92 d.

Degradation under dark anaerobic conditions was investigated in one study with one soil (pH 7.8, clay 13.4 %, OC 0.54 %). After 14 d of aerobic incubation the samples were converted to anaerobic conditions. No new metabolites were identified under these conditions. CO_2 amounted up to 53 % AR at the end of the study (14 d aerobic + 60 d anaerobic).

A study was carried out to determine the photolytic degradation of methomyl under natural sunlight in one dry soil under non sterile conditions. No new soil metabolites were identified in this study. Acetonitrile was detected as the major volatile metabolite. The meeting of MS experts considered that the potential environmental contamination by acetonitrile derived from the use of methomyl will be insignificant with respect to other anthropogenic sources.

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

Additionally to the studies presented under the route sections, rate of degradation of methomyl in soil was also investigated in the studies presented in the thiodicarb dossier where methomyl appears as a metabolite. These studies were summarized by the rapporteur Member State in the methomyl DAR. In general these studies show that methomyl is low or moderate persistent in soil under aerobic laboratory conditions ($DT_{50\ lab\ 20\ ºC}$ = 4 – 15.2 d). However, one of the thiodicarb studies performed in

a sandy loam soil (pH 5.6, OM 0.49 % AR) at 25 ºC showed longer halve lives for thiodicarb (DT_{50} = 3.6 d) and methomyl (DT_{50} = 31 d) (Feung and Weisbach, 1991c). Whereas the study was considered initially valid by the rapporteur Member State, the applicant argued that the atypical low water content of this soil made this study not suitable for the use in the risk assessment. These arguments were presented and assessed by the rapporteur Member State in the addendum to thiodicarb and discussed in the experts meeting (EPCO 16). The meeting agreed that these values should not be use for the EU risk assessment.

An aerobic soil degradation study was conducted with the metabolite methomyl oxime in three soils (pH 5.1 – 7.8, clay 6 – 10 %, OC 0.7 – 2.1 %) at 20 ºC. This metabolite was found to be very low persistent in soil (DT_{50} = 0.7 -0.9 d).

In the photolysis study performed with methomyl, degradation of methomyl was significantly faster under irradiated conditions than in the dark control but slower than in standard aerobic degradation tests. Therefore, it is expected that under normal environmental conditions microbial degradation in soil is likely to predominate over the photolytic one.

Two studies from the open scientific literature on degradation of methomyl in the saturated zone were presented in the dossier as supporting information.

Whereas not triggered by the directive, field dissipation studies are available for thiodicarb formulated either as water flowable or slow release pellets in the thiodicarb dossier. These products were applied as soil or foliar spray (water flowable) or broadcasted in soil surface before planting (pellets). When the substance was sprayed as an aqueous flowable formulation (Norris, 1991a), field degradation half lives of thiodicarb (DT_{50} = 18 d) and methomyl (DT_{50} = 18 – 43 d) were longer than the ones measured under laboratory conditions. A revision of this study presented by the applicant was assessed by the rapporteur Member State in the addendum of thiodicarb (reproduced for transparency in the addendum of methomyl). The applicant argued that this field study was performed at a significantly higher application rate (6 x 1.11 kg/ha) than the EU representative GAP for LARVIN (2 x 375 g /ha). Additionally, the study was designed to address specific weather conditions with application just prior freezing air and soil conditions in North West US. Data were reanalyzed and new approximated lower and upper limits for thiodicarb half life were calculated ($DT_{50\ field} \approx$ 4 – 8.6 d). For methomyl the revised half lifes calculated were comparable to those given in the original report ($DT_{50\ field} \approx$ 19 d – 43 d). However the average soil temperature during the period used to calculate methomyl degradation was reported to be 3 ºC. The rapporteur Member State normalized the field dissipation rates for methomyl using the average soil temperatures over the period resulting in corrected half lives in the range of those observed in laboratory studies ($DT_{50\_field\ norm\ 20\ ºC\ pF\ 2} \approx$ 6.5 – 8.5 d).

Since the half life originally used to calculate PEC in soil was derived from a study finally not considered adequate, new PEC soil were calculated and reported in an addendum. Worst case laboratory half life of 15.2 d was used. Two applications of 450 g/ha with an interval of 14 d were calculated as a worst case representative use. Interception of 60 % (corresponding to leaf development BBCH 50) was assumed for vines and 70 % (corresponding to BBCH 20 onwards was assumed for tomatoes) was assumed for vegetables. However, the proposed representative uses as given do not restrict the application to any particular growing stage. Therefore, EFSA calculated peak

PEC soil for tomatoes use considering leaf development stages (growing stages BBCH 10-19; 50 % interception) in the updated addendum.

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

Batch adsorption/desorption studies are available for methomyl and its metabolite methomyl oxime. The results for these studies indicate that methomyl (K_{foc} = 13.3 – 42.8 mL / g) and methomyl oxime (K_{foc} = 6.6 – 20 mL / g) are very high mobile in soil.

A column (3 soils) and an aged column (1 soil) leaching studies are available for methomyl. In the column leaching study methomyl in leachate represented 6.6 – 55 % AR. Methomyl oxime was observed up to 2.2 % AR in soil and 1.7 % AR in leachate. In the aged column study, the major radioactive component in the leachate (5 % AR) co-chromatographed with methomyl.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

In sterile buffer solutions at 25 °C methomyl degradation is pH dependent. Methomyl is stable at pH 5 and pH 7 but degrades at pH 9 with a DT_{50} = 36 d.[8]. Therefore, hydrolysis is not expected to contribute significantly to the degradation of methomyl in the environment.

According aqueous photolysis study available, direct photolysis is not expected to contribute to the environmental degradation of methomyl.

Methomyl is not ready biodegradable according the available study.

Two water sediment studies with a total of four dark aerobic systems incubated at 20 °C are available for methomyl. Methomyl partitions to the sediment, reaching a maximum of 11.4 % AR in the sediment after one day in one of the systems with relatively high organic carbon content (OC 5.8 %). Degradation of methomyl occurred with half lives between 2.5 to 4.8 days in the total systems. Dissipation from the water phase was between 3.5 and 5 d (due to recalculation of some values in the addendum this range changed as 3.5 to 4.5 d). Unextractable residues in the sediment reached a maximum of 20.1 % AR after 14 d declining to 14.7 % AR at the end of the study (102 d). CO_2 reached a maximum of 32.1 – 72.3 % AR at the end of the studies. Acetonitrile was found in the volatiles trap to a maximum of 27 % AR. Acetonitrile also exceeded 10 % AR in the sediment phase (max 10.2 – 10.9 % AR). The higher formation of acetonitrile in some systems seems to be associated to predominance of anaerobic conditions in the sediments of these systems. The meeting of MS experts considered that the potential environmental contamination by acetonitrile derived from the use of methomyl will be insignificant with respect to other anthropogenic sources.

$PEC_{SW\ /\ SED}$ values for parent methomyl were calculated based only in spray drift loadings and considering two categories. The first category is 'late grapes and listed tall vegetables' (i.e. tomatoes and grapes post-flowering) and the second category is 'listed low vegetables' (i.e. courgettes and aubergines). For cucumber it is necessary for Member States to consider which category cucumbers

[8] A half life of 15 d at pH 9 was reported in the thiodicarb DAR from a study performed with this substance.

fit into under their growing regimes. In all simulations a worst case half life of 5 days in water was initially assumed. The values were recalculated for a water phase half life of 4.5 d in the addendum.

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

The potential of ground water contamination by methomyl and its soil metabolite methomyl oxime was simulated by the applicant for the representative uses in vines and tomatoes with FOCUS PRZM 2.2.1 and FOCUS PEARL 1.1.1 models for all relevant scenarios. The rapporteur Member State recalculated the PEC_{GW} with the end points derived for methomyl using all the available information (including the information derived for methomyl as a metabolite of thiodicarb). A mean soil normalized half life of 7.38 d was used. Two applications of 450 g / ha per year at 14 d interval were simulated assuming 50 % crop interception for tomatoes (corresponding to grow stage BBCH 10-19 for application 30 days after emergence) and 60 % crop interception for vines (corresponding to leaf development for application 65 days after "emergence"). None of the crop / scenario combination exceeded the 0.1 µg / L on the 80th percentile annual average concentrations neither for methomyl nor for methomyl oxime. Values have not been recalculated for the slightly lower mean derived when the Feung and Weisbach (1991c) study is excluded since no change in the ground water risk assessment is expected.

4.3. FATE AND BEHAVIOUR IN AIR.

The Henry law constant of $8.6 \cdot 10^{-10}$ indicate that methomyl is unlikely to volatilize from water or wet soil. This is confirmed by the available soil volatilization study and the water / sediment studies. However, available plant volatilization study indicates that volatilization from leaves surface can occur (27 % within 24 h at 20 ºC with a relative humidity of aprox. 50 %). Photochemical degradation in the upper atmosphere is expected to occur with a half life of 19 h. Therefore, concentration of methomyl in the air compartment and transport through it is not expected to be significant.

5. Ecotoxicology

Methomyl was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 32) in September 2005 in York (UK).

Methomyl is intended to be used in cucumber/courgette, tomato/eggplant and grape (table & wine). The use in grapes is not longer supported by the applicant for the EU review process (i.e. with respect to Annex I inclusion). Nevertheless the risk from this originally intended use is reported as far as the risk assessment is available.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk to birds and mammals is calculated in the DAR based on residue data as outlined in EPPO (1992). The risk was calculated for insectivorous birds as the foliage of the crops of the intended uses

(cucumber/courgette, tomato/eggplant and grape) is considered to be a non-attractive food source to birds at the time of application. In grapes, the risk to a herbivorous mammal was assessed and for the same reason as for birds (see above) only the risk to an insectivorous mammal was assessed in cucumber/courgette and tomato/eggplant.

Based on the assessment in the DAR according to EPPO (1992) the short and long term risk to birds can be regarded as low as the TER values (303 and 11.5 respectively) exceed the corresponding Annex VI trigger value. With a TER of 2.6, the acute risk to insectivorous birds is considered to be high in the first tier risk assessment.
Some refinement options are discussed in the DAR. The rapporteur Member State considered a refinement of the acute risk via the dietary endpoint as the most appropriate way but a further clarification was considered necessary. This was provided shortly before the EPCO experts' meeting. It was noted that the PPR Panel had considered a similar issue when they assessed a question on pirimicarb[9]. The expert's meeting acknowledged that the question to be answered is basically the same as that for pirimicarb. Therefore it was decided that the applicant should be asked to address the acute risk from methomyl on the same basis as was done by the PPR Panel for pirimicarb, but it must be fully supported and all issues addressed e.g. metabolism and DT_{50} in the animal particularly in relation to the labelling position of the molecule, time to onset of toxic effect and reversibility of effects. Furthermore the meeting requested the applicant to provide a first tier risk assessment based on SANCO/4145/2000 and the dietary and reproduction endpoints for birds in terms of mg a.s./kg bw/day and a revised risk assessment.

The NOAEL for mammals was discussed in the experts' meeting. The meeting agreed to retain the endpoint of 75 ppm, based on pup weight, since no agreement on the ecological relevance of reduced pup weight could be reached. Furthermore the meeting decided that the acute endpoint from the study with the lead formulation should be used as this endpoint gives a lower value than the endpoint from the study with the a.s. The rapporteur Member State did not recalculate the acute risk to mammals based on the lowest endpoint from the study with the formulation but communicated in the evaluation table that the corresponding TER-values would be 91.33% of the available TER values. The EFSA would like to point out that this value is correct for the LD_{50} for the combined sexes but the value for female rats alone will be lower based on the mortality figures at the different concentration rates (this value is not available).
Based on the assessment according to EPPO (1992) both the acute and the long term risk to herbivorous mammals in grapes have to be regarded as high. Based on a weight of evidence approach (DT_{50} on foliage of 2 days and PD is likely to be below 1) this long term risk was considered to be addressed. The TER-values for insectivorous mammals are above the Annex VI trigger value indicating a low risk to mammals in cucumber/courgette and tomato/eggplant if calculated according to EPPO (1992). This outcome would not be altered by using the endpoint from the study with the formulation (see above).

[9] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR) on a request from EFSA related to the evaluation of pirimicarb. *The EFSA Journal* (2005) 240, 1-21.

The identified acute risk to mammals was refined in a similar way as for birds. Therefore the experts' meeting decided that the data gap for the applicant, to address the acute risk from methomyl on the same basis as was done by the PPR Panel for pirimicarb, is a data gap for birds and for mammals. The meeting had some reservations about the volume of stomach approach used by the applicant.

The EFSA recalculated the first tier risk assessment for birds and mammals according to the "Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC" (Sanco/4145/2000 of 25. September 2002) as the risk to birds and mammals was calculated according to the EPPO (1992) scheme by the rapporteur Member State. These calculations can be found in the addendum by the EFSA.
Based on this risk assessment the short term risk to birds can be regarded as low as the calculated TER value is above the respective Annex VI trigger value for the representative uses evaluated. The Annex VI trigger values for the acute and long term risk are breached indicating a high acute and long term risk to birds in the first tier risk assessment. Also a high acute and long term first-tier risk to insectivorous mammals in fruiting vegetables and herbivorous mammals in grapes was identified in this first tier risk assessment. Therefore the EFSA proposes a data gap for the applicant to submit a refinement of the long term risk to birds and mammals if the risk is assessed according to the latest guidance document (SANCO/4145/2000). For the acute risk to birds and mammals see outstanding data gap discussed above.

Furthermore the EFSA made a risk assessment for birds and mammals from consumption of contaminated drinking water available in an addendum. The acute risk to birds from consumption of contaminated drinking water is considered to be high for all representative uses evaluated. Also the short and long term risk to birds from consumption of contaminated drinking water is considered to be high for all representative uses evaluated except for birds in fruiting vegetables for which the short term risk can be considered as low. The acute and long term risk to mammals is considered to be high for all representative uses evaluated. Therefore the EFSA proposes a data requirement for the notifier to refine the risk to birds and mammals from exposure to contaminated drinking water. This assessment was neither discussed at an EPCO Experts' meeting nor peer reviewed.
A high risk from contaminated drinking water was shown from a first tier risk assessment based on worst case assumptions (e.g. the total daily water demand is taken from leaf axils or puddles which are contaminated by the sprayed solutions). Some MSs are of the opinion that long-term exposure to contaminated drinking water can be excluded and hence regard the long-term risk from uptake of contaminated drinking water as low. However, no common agreement among MSs exists yet on the potential long-term risk from contaminated drinking water. It is planned to discuss the risk to birds and mammals from uptake of contaminated drinking water as a general point at an experts' meeting.

It is considered that the risk assessment for methomyl also covers the risk assessment for the plant metabolite methomyl oxime.

As the logPow is below 3 the risk from secondary poisoning to birds and mammals is considered to be low.

5.2. RISK TO AQUATIC ORGANISMS

Daphnia magna is the most sensitive aquatic organism on an acute and chronic time-scale when tested with methomyl and the lead formulation Methomyl 20 SL. Also fish are sensitive to methomyl. The NOEC for *D. magna* is the pivotal endpoint which drives the risk assessment.

In the section on Fate and behaviour, PEC_{sw} values were calculated for two categories. The first category is 'late grapes and listed tall vegetables' (i.e. tomatoes and grapes post-flowering) and the second category is 'listed low vegetables' (i.e. courgettes and aubergines). For cucumber it is necessary for Member States to consider which category cucumbers fit into under their growing regimes.

The risk to aquatic organisms is considered to be high (*D. magna* chronic TER = 0.129-0.38). The risk can be considered as low if risk mitigation measures such as a buffer zone of 50 metres is taken into account for 'late grapes and listed tall vegetables' and a buffer zone of 30 metres is taken into account for 'listed low vegetables'. A case was made by the applicant for the use of time-weighted average PEC values in the risk assessment. It is considered that the use of such time weighted average PEC values could potentially underestimate the risk resulting from initial period of exposure. Therefore this approach has not been used.

No major metabolites were identified in surface water and ground water.

Methomyl was not found in concentrations above 10% of the AR in the sediment and hence a risk assessment for sediment dwelling organisms is not required. Acute studies on a number of sediment dwelling species were provided. All tested species were less sensitive to methomyl than *D. magna*.

Methomyl is not an herbicide so studies on aquatic plants are not considered necessary.

As the log Pow is below 3, no study on bioconcentration in fish is considered necessary.

5.3. RISK TO BEES

Acute contact and oral toxicity studies both with methomyl and the lead formulation are available. The resulting HQ values breach the appropriate Annex VI trigger value indicating a high risk to bees for the representative uses evaluated.

To address the observed mortality in the laboratory, two semi-field tests were submitted. The aim of both studies was to quantify the duration of harmful effects on bees following an application of methomyl at 450 g a.s./ha.

In the first semi-field study Methomyl 20 SL was applied to *Phacelia tanacetiflora* and effects on foraging honey bees exposed to spray deposits 2, 6, and 11 days after treatment were recorded. The

report concluded that there were no significant effects on mortality when residues were aged for over 2 days. However, the results need to be treated with caution since effects were greater for residues aged for 6 days than those aged for 2 or 11 days. No adverse effects on behaviour, flight activity or incidence of abnormal development were observed.

In the second semi-field study bees were exposed to spray deposits 1, 5, and 10 days after treatment in an apple orchard. Temporary harmful effects on bees were observed, if exposed 1 day after treatment and this effect was the most pronounced in the first 2 days. However, similar effects were observed from residues aged for 10 days and it was considered that the statement, that only effects were observed from 1 day old residues, was not supported. Most mortality occurred in the first 2 days of the evaluation period irrespective of the ageing period of the residues and also in the control thus making results difficult to interpret. It is possible that adverse effects may have been a consequence of the disturbance of the hives due to their introduction in the trial as effects were seen across all treatments including the control. No abnormal behaviour and no incidence for abnormal development of the bee brood were observed, due to Methomyl 20 SL.

In conclusion, a high risk to bees was observed in the laboratory. The information on the effects of aged residues in the 2 semi-field studies is of limited use in refining the risk. The risk to bees was discussed in the EPCO experts' meeting. Risk mitigation measures to avoid all contact with bees are considered necessary. No data to establish a withholding period is available.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory studies with *Aphidius rhopalosiphi* and *Typhlodromus pyri* are available during which a high toxicity to these standard indicator species was observed. In an extended laboratory study *T. pyri* and *A. rhopalosiphi* still showed a high sensitivity when exposed to fresh residues but effects were below 50% for *T. pyri* at dose rates below 40 g a.s./ha or when the in-field dose rate was aged for 7 days. Effects on *A. rhopalosiphi* were below 50% when a dose rate of 1.25 kg a.s./ha was aged for 14 days or when a protected life stage was exposed to a dose rate of 450 g a.s./ha.

Also extended laboratory studies with *Poecilus cupreus*, *Chrysoperla carnea*, *Aleochara bilineata* and *Orius laevigatus* are available in which all effects were below 30% at the in-field dose rate of 450 g a.s./ha or higher if the residues were aged for 1 to 7 days.

Several field studies with predatory mites are available. In all these studies methomyl was applied twice at a rate of 450 g a.s./ha with an interval of 14 days. Maximum effects observed were 64% reduction 28 days after the second application, 71% reduction 28 days after the second application, 93% reduction 56 days after the second application, 87% reduction 28 days after the second application and 98.7 % reduction 27 days after the second application. The first observations of effects below 50% were made after 81 days, 338 days, 371 days, 56 days and 83 days in the different field studies.

Furthermore 2 field studies at potential drift rates of 22.5 and 33.75 g a.s./ha are available. At 22.5 g a.s./ha an increase of the population of 36% and 5% was observed 8 and 27 days after treatment respectively. In the study at 33.75 g a.s./ha a non significant decrease of the population of 9% and 22% was seen at 8 and 27 days after application respectively. This means that effects were increasing until the end of the study.

The following was noted during the EPCO experts' meeting: in the extended laboratory studies with *T. pyri* effects were below 50% for 7 days aged deposits while in the field studies effects were more persistent (2 field studies showed pronounced effects for a period longer than 300 days, in 3 other studies recovery was observed within 80 days, see above). There was a concern that this might also be true for the other species tested. Only field studies with *T. pyri* are available and none with the other species tested. From laboratory studies using aged residue studies such long term effects would not be predicted but this was also the case for *T. pyri*. Therefore the experts' meeting considered that the in-field risk assessment was not fully addressed.

Furthermore several comments were made during the experts' meeting on the off-field risk assessment. Only one species was present in the field study therefore a safety factor should be used to address the lack of diversity. No multiple application factor nor a correction/leaf distribution factor have been used in the calculation of the off-field dose rate. Therefore the meeting considered also the off-field risk as unresolved.

As the in-field and off-field risk was considered not fully addressed, the experts' meeting considered that the applicant needs to refine the risk assessment for non-target arthropods for both the in-field and off-field areas.

5.5. RISK TO EARTHWORMS

Two studies on the acute toxicity of methomyl to earthworms are available. The endpoints were not corrected as the logPow is below 2. The risk assessment was revised as the PEC_{soil} values changed during the EPCO expert meeting. These new PEC_{soil} values only cover uses from growing stage BBCH 50 onwards (leaf development) for vines and BBCH 20 onwards (stem elongation) for fruiting vegetables. The rapporteur Member State presented this revised risk assessment only in the list of endpoints. For reasons of transparency, EFSA presented these calculations again in an addendum, clearly indicating which PEC_{soil} values have been used. The TER-values resulting from the endpoint derived from these studies do not breach the Annex VI trigger value (TER>51.8) indicating a low acute risk to earthworms for these late growing stages. However, representative uses originally proposed (preharvest) do not define the time of application and therefore a risk assessment for earlier stages for fruiting vegetables has been performed by the EFSA (see addendum by the EFSA). Also for the earlier stage for tomatoes the acute risk to earthworms can be regarded as low.

The DT_{90} for soil in the laboratory equals 50.5 days and the maximum number of applications equals 2. Therefore no chronic study on earthworms is required according to the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002). However a chronic toxicity study with the lead formulation Methomyl 20SL is available and therefore a chronic risk assessment was performed. This resulted in a low long term risk to earthworms for the representative use in fruiting vegetables (cucumber/courgette and tomato/eggplant) for growth stages of BBCH 20 onwards but a high risk was identified for growth stages before BBCH 20 (see addendum prepared by the EFSA). For the risk in grapes the TER value is below the Annex VI trigger value indicating a high long term risk to earthworms in grapes. Therefore the EFSA proposes that these risks should be addressed by the applicant as was originally proposed by the rapporteur Member State in the DAR.

No major metabolites were identified in soil.

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

The DT_{90} for soil in the laboratory equals 50.5 days. Under field conditions the DT_{90} soil might be shorter than this. Therefore no studies on the effects of methomyl on other soil non-target macro-organisms were considered necessary and hence the risk is considered to be low.

No major metabolites were identified in soil.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of methomyl were tested on soil microbial respiration and nitrogen transformation. No deviations of more than 25% after 28 days were observed at 0.45 and 4.5 kg methomyl/ha (i.e. no breaching of the Annex VI trigger value). These dose rates are equal or higher than the dose rates of the representative uses and hence the risk to soil non-target micro-organisms from methomyl is considered to be low for the representative uses evaluated.

No major metabolites were identified in soil.

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

A greenhouse phytotoxicity study was conducted on six plant species representing 2 families of Monocotyledonae and 3 families of Dicotyledonae. A maximum effect of 6.3% on oats was observed at 2.25 L Methomyl 20 SL/ha. This dose rate is equal to an application rate of 450 g a.s./ha, the maximum application rate of the representative uses. Therefore the risk to non-target plants is considered to be low.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The 3 hour EC_{50} for methomyl on the activity of activated sludge exceeds 100 mg/L. Based on this study the risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: methomyl

Definitions for monitoring: methomyl

Water

Ground water

Definitions for exposure assessment: methomyl

Definitions for monitoring: methomyl

Surface water

Definitions for risk assessment: methomyl

Definitions for monitoring: methomyl

Air

Definitions for risk assessment: methomyl

Definitions for monitoring: methomyl

Food of plant origin

Definitions for risk assessment: methomyl

Definitions for monitoring: methomyl

Food of animal origin

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

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

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
methomyl	Low to moderate persistent ($DT_{50\ lab\ 20\ ^oC}$ = 4 – 15.2 d)	See points 5.5, 5.6 ad 5.7.

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**
methomyl	Very high mobile (K_{foc} = 13.3 – 42.8 mL / g)	FOCUS (PRZM 2.2.1 and PEARL 1.1.1): trigger is not exceeded for any of the simulated uses and scenarios	Yes	Yes	See point 5.2.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
methomyl (water and sediment)	See point 5.2.

Air

Compound (name and/or code)	Toxicology
methomyl	T+, R26 'Very toxic by inhalation'

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

- An operator, worker and bystander risk assessment with the input parameters agreed during the EPCO meeting on toxicology is missing and therefore required (a position paper was made available in May, but has not been evaluated by the RMS; refer to point 2.12).
- A revision of the risk assessment for birds and mammals on the same basis as the opinion of the PPR Panel on pirimicarb (The EFSA Journal (2005 240, 1-21) (for birds relevant for all representative uses evaluated; if calculated according to EPPO (1992) and SANCO/4145/2000 for mammals relevant for grapes if calculated according to EPPO (1992); for mammals relevant for all representative uses evaluated if calculated according to SANCO/4145/2000; data submitted in February 2006, not evaluated; refer to point 5.1).
- A first tier risk assessment for birds and mammals according to SANCO/4145/2000 (relevant for all representative uses evaluated; data submitted in February 2006, not evaluated; refer to point 5.1).
- The dietary and reproduction endpoints for birds in terms of mg a.s./kg bw/day and a revised risk assessment (relevant for all representative uses evaluated; submission date not known; refer to point 5.1).
- A refinement of the long term risk to birds and mammals (proposed by the EFSA, not discussed at an experts' meeting) (relevant for all representative uses evaluated if the risk is assessed according to the latest guidance document (SANCO/4145/2000), submission date not known; refer to point 5.1).
- The risk to birds and mammals from exposure to contaminated drinking water needs to be addressed (relevant for all representative uses evaluated if the risk is assessed according to the latest guidance document (SANCO/4145/2000); proposed by the EFSA, not discussed at an experts' meeting; submission date not known; refer to point 5.1).
- A refinement of the risk assessment for non-target arthropods for both the in-field and off-field areas (relevant for all representative uses evaluated; data submitted in February 2006, not evaluated; refer to point 5.4).
- The long term risk to earthworms needs to be addressed (relevant for the use in grapes and the use in fruiting vegetables before growth stage BBCH 20; submission date not known; 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 insecticide comprise foliar spraying to control biting and sucking insects in cucumber, courgette, tomato and eggplants. Only the use as insecticide was evaluated. It should be noted that the use in grape was withdrawn during the EU peer review process.

The representative formulated product for the evaluation was "Methomyl 20 SL", a soluble concentrate (SL), registered in some Member States of the EU.

Adequate methods are available to monitor all compounds given in the respective residue definition. 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.

Methomyl is highly toxic via the oral, ocular and inhalation routes of exposure, but it has a low toxicity via the dermal route. On the basis of the data package available the proposed classification is T+, R26 'Very toxic by inhalation' and R25 'Toxic if swallowed'. It is not an eye or skin irritant and does not cause skin sensitisation. The overall short term NOAEL is approximately 10 mg/kg bw/day. Reliable data on effects on ChE activity were not always determined. Based on the available studies, the weight of the evidence indicates that methomyl does not pose a genotoxic, reproductive or developmental concern. There was no evidence of methomyl-induced carcinogenic activity in rats or mice. The NOAEL for acute neurotoxicity is 0.25 mg/kg bw. The ADI, AOEL and ARfD were set at 0.0025 mg/kg bw, based on the acute neurotoxicity NOAEL applying a SF of 100.
The operator, worker and bystander risk assessment should be regarded as inconclusive, since the rapporteur Member State recalculated operator, worker and bystander exposure with dermal absorption values slightly different from the ones agreed during the experts' meeting; however, the assessment is not expected to change significantly even with the use of values agreed during the experts' meeting. The operator exposure estimates exceed the AOEL in all scenarios considered.

The metabolism of methomyl in fruits is fully elucidated. Four metabolic pathways were identified generally leading to metabolites of no toxicological concern, as formed as a result of hydrolysis of the carbamate ester link and further degradation. However at least 2 metabolites were identified with intact carbamate structure (IN-HUZ57 and IN-G6520) and are considered as toxicologically relevant. In fruits, these metabolites are present at much lower levels than the parent compound and their contribution to the global toxicological burden is expected to be minor. Therefore, only the parent compound is proposed to be included in the residue definition for monitoring and risk assessment in fruit crops. For other commodities dealt with at member state level, the need for inclusion of these metabolites in the residue definition for risk assessment should be carefully considered as it appears that their ratio to the parent compound may be significant on leafy parts of plants, based on information obtained on grape foliage.
A sufficient amount of supervised residue trials were conducted in accordance with the supported representative uses, demonstrating that a MRL of 0.5 mg/kg would be needed for table and wine grapes, while residues in fruiting vegetables are consistently below the Limit Of Quantification (0.02 mg/kg) of the analysis method. In processed commodities (grape juice and wine), residues are lower than in raw grapes, this resulting from a preferential transfer to solid fractions during processing and

from a partial degradation of methomyl to methomyl oxime. This degradation product has however no toxicological relevance.

On the basis of the supported representative uses dealt with under this peer review, no livestock exposure to methomyl residues is expected. Due to the low persistency of methomyl in soil, no residue of methomyl is expected in following crops.

Acute and chronic exposure assessments to methomyl residues were performed. A potential acute risk was identified for all considered population subgroups resulting from the consumption of treated table grapes.

Degradation of methomyl under dark aerobic conditions in soil does not produce any major metabolite. Methomyl oxime was identified as a minor soil metabolite (max 2.2 % AR after 1d). Taking into consideration also studies performed with thiodicarb (where methomyl appears as metabolite) methomyl is low or moderate persistent in soil under aerobic conditions ($DT_{50\ lab\ 20\ ºC}$ = 4 – 15.2 d). Unextractable residues accounted for up to 32.2 % AR after 30 d and CO_2 for 75.4 % AR after 92 d. No new soil metabolites were identified in the soil photolysis study. Acetonitrile was detected as the major volatile metabolite. The meeting of MS experts considered that the potential environmental contamination by acetonitrile derived from the use of methomyl will be insignificant with respect to other anthropogenic sources. Under normal environmental conditions microbial degradation in soil is likely to predominate over the photolytic one.

In the available field studies for thiodicarb, field degradation half lives of thiodicarb and methomyl were longer than the ones measured under laboratory conditions. However the average soil temperature during the period used to calculate methomyl degradation was reported to be 3 ºC. The rapporteur Member State normalized the field dissipation rates for methomyl using the average soil temperatures over the period resulting in corrected half lives in the range of those observed in laboratory studies.

Since the half life originally used to calculate PEC in soil was derived from a study finally not considered adequate, new PEC soil were calculated and reported in an addendum. Worst case laboratory half life of 15.2 d was used. Two applications of 450 g/ha with an interval of 14 d were calculated as a worst case representative use. Interception of 60 % (corresponding to leaf development BBCH 50) was assumed for vines and 70 % (corresponding to BBCH 20 onwards was assumed for tomatoes) was assumed for vegetables. However, the proposed representative uses as given do not restrict the application to any particular growing stage. Therefore, EFSA calculated peak PEC soil for tomatoes use considering leaf development stages (growing stages BBCH 10-19) in the updated addendum.

According batch adsorption / desorption studies methomyl is very high mobile in soil (K_{foc} = 13.3 – 42.8 mL / g). A column (3 soils) and an aged column (1 soil) leaching studies are available for methomyl. In the column leaching study methomyl in leachate represented 6.6 – 55 % AR. Methomyl oxime was observed up to 2.2 % AR in soil and 1.7 % AR in leachate. In the aged column study, the major radioactive component in the leachate (5 % AR) co-chromatographed with methomyl.

Hydrolysis is not expected to contribute significantly to the degradation of methomyl in the environment (stable at pH 5 and 7, DT_{50} = 36 d at pH 9 in buffered water at 25 °C). Direct photolysis

is also not expected to contribute to the environmental degradation of methomyl. Methomyl is not ready biodegradable according the available study.

In water / sediment systems, methomyl partitions to the sediment, reaching a maximum of 11.4 % AR in the sediment after one day in one of the systems. Degradation of methomyl occurred with half lives between 2.5 to 4.8 days in the total systems. Dissipation from the water phase was between 3.5 and 4.5 d. Unextractable residues in the sediment reached a maximum of 20.1 % AR after 14 d declining to 14.7 % AR at the end of the study (102 d). CO_2 reached a maximum of 32.1 – 72.3 % AR at the end of the studies. The higher formation of acetonitrile in some systems seems to be associated to predominance of anaerobic conditions in the sediments of these systems. Acetonitrile was found in the volatiles trap to a maximum of 27 % AR. Acetonitrile also exceeded 10 % AR in the sediment phase (max 10.2 – 10.9 % AR). The meeting of MS experts considered that the potential environmental contamination by acetonitrile derived from the use of methomyl will be insignificant with respect to other anthropogenic sources.

$PEC_{SW\ /\ SED}$ values for parent methomyl were calculated based only in spray drift loadings and considering two categories. The first category is 'late grapes and listed tall vegetables' (i.e. tomatoes and grapes post-flowering) and the second category is 'listed low vegetables' (i.e. courgettes and aubergines). For cucumber it is necessary for Member States to consider which category cucumbers fit into under their growing regimes. In all simulations a worst case half life of 5 days in water was initially assumed. The values were recalculated for a water phase half life of 4.5 d in the addendum. The potential of ground water contamination by methomyl and its minor soil metabolite methomyl oxime was simulated by the applicant and recalculated by the rapporteur Member State for the representative uses in vines and tomatoes with FOCUS PRZM 2.2.1 and FOCUS PEARL 1.1.1 models for all relevant scenarios. None of the crop / scenario combination exceeded the 0.1 µg / L on the 80th percentile annual average concentrations neither for methomyl nor for methomyl oxime.

Methomyl is unlikely to volatilize from water or wet soil. However, volatilization from leaves surface can occur. Photochemical degradation in the upper atmosphere is expected to occur with a half life of 19 h. Therefore, concentration of methomyl in the air compartment and transport through it is not expected to be significant.

Methomyl is intended to be used in cucumber/courgette, tomato/eggplant and grape (table & wine). The use in grapes is not longer supported by the applicant for the EU review process (i.e. with respect to Annex I inclusion). Nevertheless the risk from this originally intended use is reported in the section on ecotoxicology as far as the risk assessment is available.

Based on the assessment according to EPPO (1992) the short and long term risk to birds can be regarded as low. With a TER of 2.6, the acute risk to insectivorous birds is considered to be high in the first tier risk assessment. The experts' meeting decided that the applicant should be asked to address the acute risk from methomyl on the same basis as was done by the PPR Panel for pirimicarb, but it must be fully supported and all issues addressed e.g. metabolism and DT_{50} in the animal particularly in relation to the labelling position of the molecule, time to toxic effect and reversibility of effects. Furthermore the meeting requested the applicant to provide a first tier risk assessment based on SANCO/4145/2000 and the dietary and reproduction endpoints for birds in terms of mg

a.s./kg bw/day and a revised risk assessment. Based on the assessment according to EPPO (1992) both the acute and the long term risk to herbivorous mammals in grapes have to be regarded as high. Based on a weight of evidence approach, this long term risk was considered to be addressed. The experts' meeting decided that the acute risk from methomyl should be refined by the applicant on the same basis as was done by the PPR Panel for pirimicarb. The TER-values for insectivorous mammals are above the Annex VI trigger value indicating a low risk to mammals in cucumber/courgette and tomato/eggplant if calculated according to EPPO (1992).

The EFSA recalculated the first tier risk to birds and mammals according to SANCO/4145/2000. Based on this risk assessment the short term risk to birds can be regarded as low but a high acute and long term risk was identified as well as a high acute and long term risk to mammals for all representative uses evaluated. Therefore the EFSA proposes a data gap for the applicant to submit a refinement of the long term risk to birds and mammals if the risk is assessed according to the latest guidance document (SANCO/4145/2000). For the acute risk to birds and mammals see outstanding data gap discussed above. The EFSA also calculated the first tier risk from exposure to contaminated drinking water. A risk for birds and mammals was identified which the EFSA proposes to be addressed.

A high risk to aquatic organisms was identified for which risk mitigation measures such as a buffer zone of 50 metres for 'late grapes and listed tall vegetables' and a buffer zone of 30 metres for 'listed low vegetables' should be taken into account.

A high risk to bees was identified. Risk mitigation measures to avoid all contact with bees are considered necessary. No data to establish a withholding period is available.

A high risk to non-target arthropods was identified in the laboratory. The applicant is asked to refine the risk assessment for non-target arthropods for both the in-field and off-field areas. The risk can only be concluded once this data becomes available but risk mitigation measure will possibly be necessary.

The acute risk to earthworms is considered to be low. In addition also the long term risk to earthworms can be considered as low for the representative uses in cucumber/courgette and tomato/eggplant for growth stages from BBCH 20 onwards. A long term risk to earthworms in grapes and in fruiting vegetables before growth stage BBCH 20 was identified. It is proposed that the applicant should address this risk.

The risk to soil micro-organisms, other soil non-target macro-organisms, non-target plants and biological methods for sewage treatment is considered to be low.

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

- To address the risk to aquatic organisms risk mitigation measures such as a buffer zone of 50 metres for 'late grapes and listed tall vegetables' and a buffer zone of 30 metres for 'listed low vegetables' should be taken into account (refer to point 5.2).
- Risk mitigation measures to avoid all contact with bees are considered necessary. No data to establish a withholding period is available (refer to point 5.3)
- The risk to non-target arthropods cannot be concluded yet but risk mitigation measures will possibly be necessary to address the observed toxicity (refer to point 5.4)

Critical areas of concern

- The operator, worker and bystander risk assessment should be regarded as inconclusive due to the lack of a refined calculation according to the EPCO outcomes. However, the AOEL is likely to be exceeded in all scenarios considered.
- An acute dietary risk has been identified for all considered population subgroups (including infants, toddlers, children and adults) resulting from the consumption of table grapes treated according to the proposed representative use.
- A high acute risk to birds and mammals was identified according to EPPO (1992) and SANCO/4145/2000. The EPCO meeting decided that this risk should be addressed according to the opinion of the PPR panel on pirimicarb. Furthermore a long term risk to birds and mammals was identified if the risk is calculated according to the latest guidance document SANCO/4145/2000. Therefore the EFSA proposes a refinement of the long term risk to birds if the risk is assessed according to the latest guidance document (SANCO/4145/2000). A risk for birds and mammals from consumption of contaminated drinking water was identified which the EFSA proposes to be addressed as well.
- A high risk to aquatic organisms was identified for which risk mitigation measures such as a buffer zone of 50 metres for 'late grapes and listed tall vegetables' and a buffer zone of 30 metres for 'listed low vegetables' should be taken into account.
- A high risk to bees was identified. Risk mitigation measures to avoid all contact with bees are considered necessary. No data to establish a withholding period is available.
- A high risk to non-target arthropods was identified in the laboratory. The applicant is asked to refine the risk assessment for non-target arthropods for both the in-field and off-field areas. The risk can only be concluded once the requested data is evaluated but risk mitigation measure will possibly be necessary.
- A long term risk to earthworms in fruiting vegetables before growth stage BBCH 20 was identified.

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

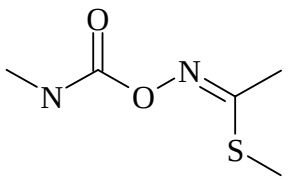
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	Methomyl (formerly DPX-X1179**)**
Function (e.g. fungicide)	Insecticide/acaricide

Rapporteur Member State	United Kingdom
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	S-methyl (EZ)-N-(methylcarbamoyloxy)thioacetimidate *Note – the cis isomer [see structure below] is so strongly favoured that the trans isomer is not detectable in practice.*
Chemical name (CA) ‡	Methyl N-[[(methylamino)carbonyl]oxy] ethanimidothioate
CIPAC No ‡	264
CAS No ‡	16752-77-5
EEC No (EINECS or ELINCS) ‡	240-815-0
FAO Specification ‡ (including year of publication)	980 g/kg [264/TC (2002)]
Minimum purity of the active substance as manufactured ‡ (g/kg)	Minimum declared 985 g/kg.
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None.
Molecular formula ‡	$C_5H_{10}N_2O_2S$
Molecular mass ‡	162.2
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) ‡	79.6 ± 0.1 °C (98.02% pure)
Boiling point (state purity) ‡	Not applicable; test material is a solid which decomposes after melting
Temperature of decomposition	192 ± 3.1°C (98.02% pure)
Appearance (state purity) ‡	Solid, white powder (98.02% pure)
Relative density (state purity) ‡	1.318 ± 0.001 g/cm^3 (1318 kg/m^3) @ 20.3 ± 0.4 °C (98.02% pure).
Surface tension	0.0737 N/m (1 mg/mL solution in water at 20.1 ± 0.3 °C) (98.02% pure)
Vapour pressure (in Pa, state temperature) ‡	5.4 x 10^{-6} mm Hg (7.2 x 10^{-4} Pa) at 25 °C (99.2% pure)
Henry's law constant (Pa m^3 mol $^{-1}$) ‡	AT 25 °C: 2.1X10^{-11} ATM M^3/MOL 2.1X10^{-6} Pa m^3/mol
Solubility in water ‡ (g/l or mg/l, state temperature)	55 g/l (25 °C) (96.2%) pH 7 only (Methomyl is non-ionising) acceptable
Solubility in organic solvents ‡ (in g/l or mg/l, state temperature)	Solubilities at 20 °C (98.02% pure): Solvent — Solubility (mg/L) Ethyl Acetate — 7.74x10^4 *n*-Heptane — 97.1 1-Octanol — 2.40x10^4 Xylene — 9.58x10^3 Acetone — >250g/kg Acetonitrile — >250g/kg Dichloromethane — >250g/kg Dimethylformamide — >250g/kg Methanol — >250g/kg
Partition co-efficient (log POW) ‡ (state pH and temperature)	K_{ow} of methomyl at 25 °C (99.3% pure): = 1.24 (log K_{ow} = 0.09). Mean of results for two concentrations, differing by a factor 10: K_{ow}= 1.14 (at 0.1 mg/mL) and 1.35 (at 1 mg/mL). No data for effect of pH (4 – 10). Case made that methomyl does not ionise in environmental pH range

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

Hydrolytic stability (DT_{50}) ‡ (state pH and temperature)	Hydrolysis of methomyl at 25 °C was studied at pH 5, 7, and 9, and at two concentrations, 10 and 100 ppm. At pH 9, methomyl hydrolysed with a half-life of ~30 days. Methomyl was stable at pH 5 and 7. The hydrolysis product at pH 9 was IN-X1177 (methomyl-oxime, S-methyl N-hydroxythioacetimidate)
Dissociation constant ‡	Not applicable. Methomyl does not ionise at environmentally relevant pH.
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	UV / VIS absorbance maximum for acidic, basic, and neutral solutions of methomyl was 234 nm (25 °C). pH 1.74: λ_{max} 234, ε 8.98×10^3, log ε 3.95 pH 10.92: λ_{max} 234, ε 8.89×10^3, log ε 3.95 pH 7.02: λ_{max} 234, ε 9.01×10^3, log ε 3.95 No absorption maxima beyond 290 nm were observed (all pH conditions). Solutions in methanol at higher concentrations measured over a longer cell path length also showed no absorption maxima beyond 290 nm. No effect of pH on absorbance / λmax for time periods up to 30 min.
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	Methomyl does not undergo direct photolysis. Methomyl does not absorb the energy of sunlight at wavelengths ~290 nm and above. Indirect aqueous photolysis was observed in the presence of nitrate
Quantum yield of direct phototransformation in water at λ > 290 nm ‡	Not applicable. Methomyl does not absorb the energy of sunlight at wavelengths ~290 nm and above.
Flammability ‡	Not classified as highly flammable
Explosive properties ‡	Not classified as explosive

‡ 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)	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)
Cucumber/ Courgette	Southern Europe	Methomyl 20 SL	F	Biting and sucking insects	SL	200 g/L	MV/HV; foliar	Pre-harvest	1-2	14	0.025 - 0.09	500 - 1000	0.25 - 0.45	7	[1] [2]
Tomato/ Eggplant	Southern Europe	Methomyl 20 SL	F	Biting and sucking insects	SL	200 g/L	MV/HV; foliar	Pre-harvest	1-2	14	0.025 - 0.09	500 - 1000	0.25 - 0.45	7	[1] [2]
Grape (table & wine)	France (North and South Europe	Methomyl 20 SL	F	Biting and sucking insects	SL	200 g/L	HV; foliar	Pre-harvest	1-2	14	0.08 - 0.12	300 - 450	0.35	14	[1] [2] [3] [4]
Grape (table & wine)	France (North and South Europe	Methomyl 20 SL	F	Biting and sucking insects	SL	200 g/L	HV; foliar	Pre-harvest	1-2	14	0.04 - 0.10	> 450 - 1200	0.45	14	[1] [2] [3] [4]

[1] The risk assessment has revealed a data gaps and risks (exceedance of relevant threshold) in section 5.
[2] The operator, worker and bystander risk assessment should be regarded as inconclusive due to the lack of a refined calculation according to the EPCO outcomes; however, it is expected to exceed the AOEL
[3] An acute dietary risk for the consumer has been identified.
[4] The risk assessment was not completed since the applicant does not support this use for the review at EU-level.

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

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)	Reversed-phase HPLC with UV detection (235nm)
Impurities in technical as (principle of method)	Reversed-phase HPLC with UV detection (230nm)
Plant protection product (principle of method)	Reversed-phase HPLC with UV detection (235nm)

Analytical methods for residues (Annex IIA, point 4.2)

Unless otherwise stated, residue methods and associated LOQs refer to determination of parent methomyl.

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Reversed-phase HPLC with post-column derivatisation (phthalaldehyde/mercaptoethanol reaction) and fluorescence detection (Ex. 330 nm, Em. 466 nm) LOQ: 0.01 mg/kg for wide range of commodities. Confirmation by reversed-phase HPLC-MS (single ion monitoring) to LOQ of 0.01 mg/kg for acceptable range of crops.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	*Submitted but not required – no residue definition is set for food of animal origin. Not evaluated.*
Soil (principle of method and LOQ)	Reversed-phase HPLC with post-column derivatisation (phthalaldehyde/mercaptoethanol reaction) and fluorescence detection (Ex. 330 nm, Em. 466 nm). LOQ 0.001 mg/kg. ELISA with UV detection also available to validated LOQ of 0.025 mg/kg. The above methods serve interchangeably as monitoring / confirmatory methods
Water (principle of method and LOQ)	Analytical methods as for soil (HPLC-fluorescence and ELISA-UV detection) but with lower LOQs. Ground w. LOQ 0.1 µg/L Surface w. LOQ 0.25 µg/L
Air (principle of method and LOQ)	Reversed-phase HPLC with MS detection (single ion *m/z* 163). LOQ 0.58 µg/m^3 Confirmation by conversion of residues to methomyl oxime and determination by reversed-phase HPLC-MS (single ion, *m/z* 106).

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

Body fluids and tissues (principle of method and LOQ)	Residues converted to methomyl oxime and determined by GC/MS (m/z 88 for monitoring; *m/z* 58 and *m/z* 105 for confirmation. LOQ 0.01 mg/kg Additional confirmation by GC-FPD: LOQ 0.01 mg/kg

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	None for the active substance

‡ 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 ‡	Rapid after gavage administration with peak effects seen 0.5 to 3 hours post dosing. Absorption >90% in the rat and approximately 75% in the monkey (urine and expired air, 5 mg/kg bw).
Distribution ‡	Rat: Widespread (highest levels in the gastro-intestinal tract, liver, blood, and skin).
	Monkey: Widespread (highest levels in fat and muscle).
Potential for accumulation ‡	Although the radioactive tissues residues appear to be high at 168 hours, (8-9% in the rat & approximately 5% in the monkey), methomyl is broken down into small carbon compounds which join the pool of naturally occurring carbon compounds and are incorporated into the tissues.
Rate and extent of excretion ‡	Radiolabel was rapidly excreted in expired air and urine (within 24 hours of dosing (80% in the rat and 63% in the monkey) and extensive elimination in the rat at 168 hours post dosing (approximately 91%). In the monkey, approximately 75% eliminated at 168 hours post dosing.
Metabolism in animals ‡	Three major pathways were proposed: displacement of *S*-methyl from *syn*-methomyl by glutathione followed by transformation to the mercapturic acid derivative (18% of the dose); conversion of methomyl to methomyl oxime (MHTA or IN-X1177) and CO_2 release; and isomerisation of *syn*-methomyl to *anti*-methomyl (IN-B1884), followed by a Beckmann rearrangement and formation of acetonitrile.
Toxicologically significant compounds ‡ (animals, plants and environment)	Methomyl, INHUZ57, (ING6520)

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	30 mg/kg bw	**T, R25**
Rat LD_{50} dermal ‡	>2000 mg/kg bw	
Rat LC_{50} inhalation ‡	0.215 mg/l in male & females	**T+, R26**
Skin irritation ‡	Non-irritant (Not classified)	
Eye irritation ‡	Slight-irritant (Not classified)	

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

Skin sensitization ‡ (test method used and result)	Negative in a Buehler (Not classified).

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Decreases in body weight and changes in the haematological parameters.
Lowest relevant oral NOAEL / NOEL ‡	Overall NOAEL of approximately 10 mg/kg bw/day from dietary studies in rats, dogs and mice. Reliable data on effects on ChE activity not always determined.
Lowest relevant dermal NOAEL / NOEL ‡	90 mg/kg bw/day (rabbit, 21 days).
Lowest relevant inhalation NOAEL / NOEL ‡	No data submitted.

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	*In vitro:* negative. *In vivo*: negative.

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

Target/critical effect ‡	Histopathology in kidney and spleen.
Lowest relevant NOAEL / NOEL ‡	3 mg/kg bw/day (2 year dog study)
Carcinogenicity ‡	No evidence of carcinogenic activity in rats or mice.

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Parental: reduced body weight and food consumption Reproductive: no effects Offspring: reduced pup weight
Lowest relevant reproductive NOAEL / NOEL ‡	Parental: 4.6 mg/kg bw/day Reproductive: 80 mg/kg bw/day Offspring: 4.6 mg/kg bw/day
Developmental target / critical effect ‡	Maternal: Deaths, reduced body weight and clinical signs of toxicity (rabbit study) Developmental: no effects

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

Lowest relevant developmental NOAEL / NOEL ‡	Maternal: 6 mg/kg bw/day (rabbits) Developmental: 16 mg/kg bw/day (rabbits, highest dose tested)

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

Acute neurotoxicity (gavage administration)	NOAEL: 0.25 for males and females, respectively. Reversible RBC and brain cholinesterase inhibition (≥20%) at the next highest dose.
Short-term neurotoxicity (dietary administration).	NOAEL: 9.42 mg/kg bw/day for males and females, respectively. Reduced body weight and food consumption, clinical signs, brain cholinesterase inhibition and effects on FOB parameters at the next highest dose.
Delayed neurotoxicity.	No evidence for this effect was seen in the hen test.

Other toxicological studies ‡ (Annex IIA, point 5.8)

Acute dietary study in male rats	NOAEL 1 mg/kg bw (30 ppm). RBC cholinesterase inhibition (>20%) and no reaction to tail pinch at 60 ppm, the next highest dose.
IN HUZ57	No data available
IN G6520	No data available

Medical data ‡ (Annex IIA, point 5.9)

Worker monitoring data.	The company's acceptable worker exposure limit (AEL) for methomyl is 2.5 mg/m^3 (8-hours time weighted average).
Human volunteer study (acute oral/capsule)	NOAEL: 0.1 mg/kg bw. Reversible RBC and cholinesterase inhibition (≥20%) and increased salivation at 0.2 mg/kg bw, the next highest dose.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.0025 mg/kg bw/day	Acute Neurotoxicity in Rat	100
AOEL ‡	0.0025 mg/kg bw/day	Acute Neurotoxicity in Rat	100

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

ARfD ‡ (acute reference dose)	0.0025 mg/kg bw/day	Acute Neurotoxicity in Rat	100

Dermal absorption (Annex IIIA, point 7.3)

In vivo rat study using Methomyl 20 SL formulation.	EPCO Sep 05: Values of 12.5% and 2.5% are proposed for the in-uses dilution and concentrate, respectively, based on in vivo rat data corrected for rat and human in vitro data (Methomyl 20SL) March 2006: the RMS reconsidered these values, which were based on the *in vivo* rat data but corrected by a rabbit:human peak flux data instead of rat:human peak flux data. Therefore, the RMS considered more appropriate that the rat in vivo/in vitro rat:human data should be used to determine the dermal penetration values, i.e. 14% for the aqueous dilution and 0.4% for the concentrate. This proposal was not peer reviewed by MSs.

Acceptable exposure scenarios (including method of calculation) [1)]

Operator	The operator risk assessment should be regarded as inconclusive due to the lack of a refined calculation according to the EPCO outcomes; however, the exposure estimate is expected to exceed the AOEL in all scenarios considered
Workers	The worker risk assessment should be regarded as inconclusive due to the lack of a refined calculation according to the EPCO outcomes.
Bystanders	The bystander risk assessment should be regarded as inconclusive due to the lack of a refined calculation according to the EPCO outcomes.

[1)] EFSA notes that the RMS did not perform recalculations with the dermal absorption values agreed during the experts' meeting; however, the assessment is not expected to change significantly even with the use of values agreed during the experts' meeting.

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	T+; Very toxic R25, Toxic if swallowed R26 Very toxic by inhalation

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

Appendix 1.4: Residues

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

Plant groups covered	Fruit (grapes)
Rotational crops	No data submitted. Significant residues in succeeding crops unlikely due to behaviour of methomyl in soil.
Plant residue definition for monitoring	Methomyl (for fruiting crops only)
Plant residue definition for risk assessment	Methomyl (for fruiting crops only)
Conversion factor (monitoring to risk assessment)	Not required

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

Animals covered	Goat, hen.
Animal residue definition for monitoring	Not applicable (no exposure of livestock expected).
Animal residue definition for risk assessment	Not applicable (no exposure of livestock expected).
Conversion factor (monitoring to risk assessment)	Not applicable (no exposure of livestock expected).
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

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

.....	Not required. Significant residues in succeeding crops unlikely due to behaviour of methomyl in soil.

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

.....	Methomyl residues are stable in the following commodities: Grapes: up to 27 months at $\leq$ -20 °C. Raisin & grape juice: up to 8 months at $\leq$ -18 °C. Wine: up to 11 months at $\leq$ -18 °C. Broccoli & lettuce: up to 24 months at $\leq$ -20 °C. Potato, bean seed & peanut: up to 26 months at $\leq$ -20 °C. Milk: up to 181 days at $\leq$ -70 °C. Liver: up to 165 days at $\leq$ -70 °C. Cow Muscle: up to 181 days at $\leq$ -70 °C.

‡ 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	Exposure to methomyl residues through consumption by livestock of crops covered by representative uses is negligible. A ruminant feeding study was submitted and evaluated. All residues in all commodities were < 0.01 mg/kg at dose rates of 34 and 86 mg/kg feed DM. A poultry feeding study was not submitted.		

‡ 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 (a)	Recommendation/comments	MRL	STMR (b)
Grapevine	N. and S. EU	1 x 0.02, 2 x 0.03, 3 x 0.05, 2 x 0.06, 2 x 0.07, 1 x 0.09, 1 x 0.10, 1 x 0.11, 1 x 0.13, 1 x 0.18, 1 x 0.20, 1 x 0.21, 1 x 0.26, 1 x 0.28, 1 x 0.33, 1 x 0.59.		0.5	0.090
Cucumber	S. EU	6 < 0.02.	Sufficient trials to propose MRL when considered with courgette data	0.02*	0.02
Courgette	S. EU	3 < 0.02.	Sufficient trials to propose MRL when considered with cucumber data	0.02*	0.02
Tomato	S. EU	9 < 0.02.	Extrapolation to aubergine acceptable.	0.02*	0.02

(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	0.0025 mg/kg
TMDI (% ADI) (European diet)	Grapes - 0.000116 mg/kg bw/day (5%) Tomato - 0.000019 mg/kg bw/day (<1%) Aubergine - 0.000001 mg/kg bw/day (<1%) Cucumber & gherkin - 0.000003 mg/kg bw day (<1%) Fruiting veg., cucurbits - 0.000011 mg/kg bw/day (<1%) Total: 0.000161 mg/kg bw/day (6%)
NEDI (% ADI) according to diet of 10 consumer sub-populations in UK	Critical consumers = vegetarians: 0.000511 mg/kg bw/day (20%).
Factors included in NEDI	STMR - Processing factor of 0.58 for production of wine from grapes
ARfD	0.0025 mg/kg
NESTI (% ARfD) according to large portion consumption data for 10 consumer sub-populations in UK	Table grape: critical consumer (UK diet) = toddler: 0.0360 mg/kg bw/day (**1400%**). Wine: critical consumer (UK diet) = vegetarian: 0.0012 mg/kg bw/day (48%). Tomato: critical consumer (UK diet) = infant: 0.0010 mg/kg bw/day (40%). Aubergine: critical consumer (UK diet) = 4 – 6yr old child: 0.0005 mg/kg bw/day (20%). Cucumber: critical consumer (UK diet) = toddler: 0.0006 mg/kg bw/day (24%). Courgette: critical consumer (UK diet) = toddler: 0.0009 mg/kg bw/day (36%).
Factors included in NESTI	Table grapes: HR (which is above the proposed MRL), variability factor 5; Wine: STMR, no variability factor Fruiting vegetables: MRL, variability factor 7 for tomatoes and courgette and 5 for aubergines and cucumbers

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

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Grape/ grape juice	4	0.21	Not calculated
Grape/ young wine	4	0.71	Not calculated
Grape/ mature wine	4	0.58	Not calculated
Grape/ raisin	4	0.20	Not calculated

* 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)

Table and wine grapes	0.5 mg/kg
Cucumber	0.02* mg/kg
Courgette	0.02* mg/kg
Tomato	0.02* mg/kg
Aubergine	0.02* mg/kg

*) LOQ

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

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	75% at 92 days [14C-1]-label n=1
Non-extractable residues after 100 days ‡	14% at 92 days [14C-1]-label n=1
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	None major >10%AR

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

Anaerobic degradation ‡	Mineralisation 23.4% of applied 60 days after conversion to anaerobic conditions (excludes the 29% CO2 produced in the first 14 days under aerobic conditions). Non-extractable residues 24.5% 60 days after conversion. No major soil metabolites formed.
Soil photolysis ‡	Mineralisation and non-extracted residues minimal. No major soil metabolites. The major breakdown product identified was the volatile acetonitrile representing up to 40% AR at 30 days (study end).

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

Method of calculation	Simple first order kinetics, linear regression
Laboratory studies ‡ (range or median, with n value, with r^2 value)	Methomyl [data derived from thiodicarb studies also used] DT_{50lab} (20°C, aerobic): 4- 9.9 days, (n=7, r2 = 0.97-1.00). DT_{50lab} (25°C, aerobic): 10.5 days (n=1, r2 = 0.99). For FOCUS gw modelling- Parent (aerobic, 1st order) median 5.81 days. Normalised to 20ºC, –10kPa. For PECsoil longest aerobic 1st order DT_{50} normalised to 20ºC, –10kPa is 15.2 days Minor (2.5%AR) metabolite methomyl oxime DT_{50lab} (20°C, aerobic): 0.7-0.9 days, (n=3, r2 = 0.81-0.98). For FOCUS gw modelling- (aerobic, 1st order) geometric mean 0.67 days. Normalised to 20ºC, –10kPa.

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

	Methomyl DT_{90lab} (20°C, aerobic): 4-33 days, (n=7, r^2 = 0.97-1.00). DT_{90lab} (25°C, aerobic): 35 days (n=1, r^2 = 0.99). Longest DT_{90} normalised to 20ºC, –10kPa is 50.5 days Minor (2.5%AR) metabolite Methomyl oxime DT_{90lab} (20°C, aerobic): 3-4 days, (n=3, r^2 = 0.81-0.98). Methomyl DT_{50lab} (10°C, aerobic): 3 days (n=1, r^2 = 0.99) Methomyl DT_{50lab} (25°C, anaerobic): (total system) 14 days (n=1, r^2 = 0.98).
	degradation in the saturated zone: laboratory incubations using subsoils under anaerobic conditions at 10°C gave 1st order $DT_{50} \leq 8$ hours (n=5, r2 not reported)
Field studies ‡ (state location, range or median with n value)	DT_{50f}: None submitted, none required. Field studies are available for thiodicarb where methomyl appears as metabolite. See thiodicarb DAR and EFSA conclusion (list of end points). DT_{90f}: None submitted, none required
Soil accumulation and plateau concentration ‡	Requirement not triggered. Data not required

Methomyl oxime =Z-methyl N-hydroxyethanimidothioate, INX1177

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	Methomyl K_{foc} 13.3-42.8 mL/g (mean 25.2 mL/g, (1/n) = 0.82-0.89 n=5) No pH relationship observed For FOCUS gw modelling- Mean 25.2 mL/g, 1/n 0.86 Minor (2.5%AR) metabolite Methomyl oxime K_{foc} 6.6-20 mL/g (mean 11.4 mL/g, (1/n) = 0.68-0.95 n=5) No pH relationship observed For FOCUS gw modelling- Mean 11.4 mL/g, 1/n 0.78

‡ 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 ‡	Guideline: BBA part IV, 4-2 Precipitation (mm): 200 Time period (days): 2 n=3 Leachate:2-57%AR, 5.4-55%AR as methomyl 0.8-1.7%AR methomyl oxime.
Aged residues leaching ‡	Guideline: BBA part IV, 4-2 Aged for (days) 13 days Precipitation (mm): 200 Time period (days): 2 n=1 Leachate:6.7%AR, 4.7-5.3%AR as methomyl 0.8-0.9%AR methomyl oxime.
Lysimeter/ field leaching studies ‡	None submitted. None required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	DT_{50}: 15.2 days, simple 1st order kinetics longest lab value. Soil depth 5cm, soil bulk density 1.5g/cm^3
Application rate	2 x 450g methomyl/ha with 14 days interval assuming 60% crop interception (vines).

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		-	-	0.367	0.367
Short term	24h			0.350	0.359
	2d			0.335	0.351
	4d			0.306	0.335
Long term	7d			0.267	0.314
	28d			0.102	0.207
	50d			0.038	0.144
	100d			0.004	0.080

For applications at growth stages after flowering in grapes 70% crop interception is appropriate. In this situation the initial PEC is 0.275 mg/kg. For fruiting vegetables uses, 70% crop interception would correspond to applications at growing stages BBCH 20 onwards and 50 % for growing stages BBCH 10-19. For the 450g/ha

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

use pattern on fruiting vegetables an initial PEC is 0.275 mg/kg for BBCH > 20) and initial PEC is 0.458 mg/kg for BBCH 10-19

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)	pH5__: 25°C stable pH7__: 25°C stable pH9__: 25°C 1st order DT_{50} 36 days (graphical estimate) After 30 days methomyl oxime accounted fore *ca.* 42%AR
Photolytic degradation of active substance and relevant metabolites ‡	No direct aqueous photolysis (no adsorption maxima > 290nm)
Readily biodegradable (yes/no)	No
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡ - DT_{50} whole system ‡ - DT_{90} whole system ‡	 1.3-4.5 days 4.3-14.9 days (1^{st} order r^2=0.85-0.99, n=6) 2.5 4.8 days 8.2-16 days (1^{st} order r^2=0.95-0.99, n=4)
Mineralization	32&46% AR at 102 days (n=2) 72%AR at 31 days (n=1) and 60%AR at 44 days (n=1) all values at study end.
Non-extractable residues	10&15% AR at 102 days (n=2) 15.5%AR at 31 days (n=1) and 15.2%AR at 44 days (n=1) all values at study end.
Distribution in water / sediment systems (active substance) ‡	Concentrations of extractable methomyl in sediment were minimal in 3 of the systems studied (<6.2%AR at all time points). In the 5.8%oc silty clay loam system methomyl was 11.4%AR 2 days after application declining rapidly to <0.4%AR by day 14.
Distribution in water / sediment systems (metabolites) ‡	No major metabolites accumulated in the water or sediment of the systems (acetonitrile is a transient sediment component only). In addition to CO_2, the predominant breakdown products identified (acetonitrile and acetamide) are volatile.

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

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

Parent

Method of calculation	DT_{50}:4.5 days, 1st order, longest water phase dissipation DT50 from dark 20°C lab. Sediment water study.
Application rate	Crop: 1.late applications to grapes and tall growing vegetables 2.low growing vegetables both 2 applications at 14 day intervals at 450g a.s./ha to 30cm deep static water body
Main routes of entry	7.23% drift from 3m for 2 applications 2.77% drift from 1m for 1 application (as concentration is higher than from 2 applications and 2.38% drift)

$PEC_{(sw)}$ (µg / L)		1. Grapevines late and tall vegetables Actual	1. Grapevines late and tall vegetables Time weighted average	2. low growing vegetables Actual	2. low growing vegetables Time weighted average
Initial		12.1	12.1	4.15	4.15
Short term	24h	10.4	11.2	3.56	3.85
	2d	8.90	10.4	3.05	3.58
	4d	6.53	9.03	2.24	3.10
Long term	7d	4.12	7.40	1.41	2.54
	14d	1.40	4.96	0.48	1.70
	21d	0.16	2.77	0.06	0.95
	28d	0.01	1.57	0.00	0.54
	42d	0.00	0.79	0.00	0.27

Applications as above but with lower drift inputs with no spray zones required to demonstrate acceptable aquatic risk.	1. 0.1% drift from 50m for 1 application 2. 0.1% drift from 30m for 1 application (as concentrations are higher than from 2 applications and 0.08% drift)

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

PEC$_{(sw)}$ (µg / L)	1. Grapevines late and tall vegetables Actual	1. Grapevines late and tall vegetables Time weighted average	2. low growing vegetables Actual	2. low growing vegetables Time weighted average
Initial	0.15	0.15		
Short term 24h	0.13	0.14	PEC are the same as for 1.	PEC are the same as for 1.
2d	0.11	0.13		
4d	0.08	0.11		
Long term 7d	0.08	0.09		
14d	0.02	0.06		
21d	0.00	0.03		
28d	0.00	0.02		
42d	0.00	0.01		

PEC (sediment)

Parent

Method of calculation	11.4% partitioning to top 5cm layer of sediment, entry route as for surface water, pattern of decline reflecting that measured in the sediment/water study
Application rate	Crop: 1.late applications to grapes and tall growing vegetables 2.low growing vegetables both 2 applications at 14 day intervals at 450g a.s./ha to 30cm deep static water body with 5cm underlying sediment with density 1.3g/cm^3 with baseline distances of 3 and 1m respectively.

PEC$_{(sed)}$ (µg / kg)	1. Grapevines late and tall vegetables Actual	1. Grapevines late and tall vegetables Time weighted average	2. low growing vegetables Actual	2. low growing vegetables Time weighted average
Initial	-	-	-	-
Short term	Peak 6.3 at 2 days	-	Peak 2.19 at 2 days	-
Long term	< 0.22, 12 days after peak	-	< 0.08, 12 days after peak	-

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

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	For FOCUS gw modelling, values used- [data derived from studies conducted with thiodicarb also used] Modelling using FOCUS PRZM 2.4.1 and FOCUS PEARL 1.1.1 with appropriate FOCUS scenarios, according to FOCUS guidance on Grapes and Tomatoes Geometric mean DT50 lab: methomyl 7.38d (NB: revised median value would be 5.81d), methomyl oxime 0.67d normalised to –10kPa, 20°C with Q10 2.2, 100% formation of methomyl from methomyl oxime. Kfoc mean: methomyl 25.2mL/g 1/n=0.86 methomyl oxime 11.4mL/g 1/n=0.78
Application rate	2x450g a.s./ha 14 day application intervals with 60% crop interception for grapes and 50% crop interception for tomatoes 1st applications 65 days after 'emergence' for grapes and 30 days after 'emergence' for tomatoes

PEC$_{(gw)}$

Maximum concentration	-
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Annual average concentrations (80th % year) according to FOCUS guidance, see results in table below.

PEC(gw) - FOCUS modelling results

	Scenario	Parent (µg/L)	Metabolite methomyl oxime (µg/l)
PRZM 2.4.1 / Vines	Chateaudun	<0.001	<0.001
	Hamburg	0.003	<0.001
	Kremsmunster	0.001	<0.001
	Piacenza	<0.001	<0.001
	Porto	<0.001	<0.001
	Sevilla	<0.001	<0.001
	Thiva	<0.001	<0.001

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

PEARL 1.1.1 / Vines	Scenario	Parent (µg/l)	Metabolite methomyl oxime (µg/l)
	Chateaudun	0.003	<0.001
	Hamburg	0.001	<0.001
	Kremsmunster	0.001	<0.001
	Piacenza	0.084	0.005
	Porto	<0.001	<0.001
	Sevilla	<0.001	<0.001
	Thiva	<0.001	<0.001
PRZM 2.4.1 / Tomato	Scenario	Parent (µg/l)	Metabolite methomyl oxime (µg/l)
	Chateaudun	<0.001	<0.001
	Piacenza	<0.001	<0.001
	Porto	<0.001	<0.001
	Sevilla	<0.001	<0.001
	Thiva	<0.001	<0.001
PEARL 1.1.1 / Tomato	Scenario	Parent (µg/l)	Metabolite methomyl oxime (µg/l)
	Chateaudun	0.003	<0.001
	Piacenza	0.042	0.002
	Porto	<0.001	<0.001
	Sevilla	<0.001	<0.001
	Thiva	<0.001	<0.001

NOTE: The revised median methomyl DT_{50} value would be 5.81d based on addendum 1. Since an acceptable groundwater assessment was produced with the longer DT_{50} of 7.38d in the original DAR the figures above have not been amended here to reflect the agreed shorter DT_50.

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 Latitude: ..... Season: ..... DT_{50} .....
Quantum yield of direct phototransformation	Methomyl has no absorption maxima >290nm
Photochemical oxidative degradation in air ‡	Tropospheric half life of 19 hours derived by the Atkinson method of calculation for reaction with OH radicals

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

Volatilization ‡	From plant surfaces: up to 27%AR volatilised from bean leaves within 24 hours (20°C, 50% relative humidity) from soil: only 3%AR volatilised from soil within 24 hours

PEC (air)

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law coefficient and information on volatilisation from plants and soil and effect of mixing and diffusion

$PEC_{(a)}$

Maximum concentration	Negligible

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	Soil Definitions for risk assessment: methomyl Definitions for monitoring: methomyl Water Ground water Definitions for exposure assessment: methomyl Definitions for monitoring: methomyl Surface water Definitions for risk assessment: methomyl Definitions for monitoring: methomyl Air Definitions for risk assessment: methomyl Definitions for monitoring: methomyl

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

Soil (indicate location and type of study)	No pertinent information available by the notifier or in published literature

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

Surface water (indicate location and type of study)	No pertinent information available by the notifier or in published literature
Ground water (indicate location and type of study)	No pertinent information available by the notifier or in published literature
Air (indicate location and type of study)	No pertinent information available by the notifier or in published literature

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Candidate for R53: May cause long-term adverse effects to the aquatic environment

‡ 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 ‡	Methomyl: LD_{50} = 30 mg/kg bw Methomyl 20L LD_{50} = 27.35 mg a.s./kg bw (combined sexes)
Long term toxicity to mammals ‡	Methomyl NOAEL pup growth and development = 75ppm
Acute toxicity to birds ‡	Methomyl: LD_{50} = 24.2 mg/kg bw (northern bobwhite quail) (Report No. HLO 464-83) Methomyl 20SL LD_{50} = 30.4 mg/kg bw (northern bobwhite quail)
Dietary toxicity to birds ‡	Methomyl: LC_{50} =3952 mg/kg diet (mallard duck; Report No. DuPont-4379)
Reproductive toxicity to birds ‡	Methomyl: NOEC = 150 mg/kg diet (mallard duck and northern bobwhite quail; Reports nos. HLO 336-91 and HLO 337-91)

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

The risk is calculated according to EPPO (1992). Further data to refine the risk is required.

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.45 (x2)	Grapevine & fruiting vegetables	Insectivorous bird	Acute	**2.6**	10
			Short-term	303	10
			Long-term	11.5	5
0.25 (x2)	Listed fruiting vegetables[2]		Acute	**4.6**	10
			Short-term	545	10
			Long-term	21	5
0.45 (x2)	Grapevine	Herbivorous mammal	Acute	**2.3**	10
			Long-term	4.2[1]	5
0.25 (x2)	Listed fruiting vegetables	Insectivorous mammals	Acute	34	10
			Long-term	61	5

[1] The long term risk is considered acceptable based on a DT_{50} on foliage of 2 days and the fact that the diet is unlikely to be 100% treated vegetation. Residue data showed that the maximum residue 3 DAT2 was only 11 mg a.s./kg giving a TER of 6.8 i.e. > trigger value. In addition it should be noted that the NOAEL for pup survival was 600 ppm.

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

[2] The listed fruiting vegetables referred to here and subsequently are cucumber, courgette, tomato, aubergine. The metabolite methomyl oxime was considered to be covered by the risk assessment for the active substance.

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 ‡				
Acute, static – bluegill sunfish (Report No. SPL 282/571)	Methomyl	96-hour	LC_{50}	**0.63**
Acute, static – bluegill sunfish (Report No. HLR 30-91)	Methomyl 20SL	96-hour	LC_{50}	1.1
Fish early life stage – fathead minnow (Report No. HLO 702-91)	Methomyl	-	NOEC	**0.073**
Fish life cycle – fathead minnow (Report No. HLO 47-93)	Methomyl	-	NOEC	0.076
Acute, static-renewal *D. magna* (Report No. SPL 282/572)	Methomyl	48-hour	EC_{50}	**0.017**
Acute, static-renewal *D. magna*, neonates and adults (Report No. DuPont-3726)	Methomyl 20SL	48-hour	EC_{50}	0.0193 (<24-hour old *D. magna*) 0.0362 (12-day old *D. magna*)
Daphnia magna	Methomyl 20SL	48 hr	EC_{50}	28-day old adult > 0.123
Daphnia magna	Methomyl 20SL	96 hr	EC_{50}	27-day old adults = 0.098; neonate = 0.084
			NOEC	0.026
Gammarus italicus	Methomyl	96 hr	EC_{50}	0.047
Echinogammarus tibaldii	Methomyl	96 hr	EC_{50}	0.250
Daphnia longispina	Methomyl	96 hr	EC_{50}	0.220
Cyclops strenuous	Methomyl	96 hr	EC_{50}	0.190
Gammarus pulex	Methomyl	96 hr	EC_{50}	0.760
Biomphalaria alexandrina	Methomyl	96 hr	EC_{50}	1.10
Bulinus truncatus	Methomyl	96 hr	EC_{50}	0.870

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Pteronarcella badia	Methomyl	96 hr	EC_{50}	0.060
Skwala sp.	Methomyl	96 hr	EC_{50}	0.029
Gammarus pseudolimnaeus	Methomyl	96 hr	EC_{50}	1.050
Isogenus sp.	Methomyl	96 hr	EC_{50}	0.343
Chironomus sp.	Methomyl	96 hr	EC_{50}	0.032
Chironomus plumosus	Methomyl	96 hr	EC_{50}	0.088
Life-cycle, static-renewal *D. magna* (Report No. HLR 46-82)	Methomyl	21-day	NOEC	**0.0016**
Aquatic algae, *S. capricornutum* (Report No. SPL 282/573)	Methomyl	72-hour	EC_{50}	**>100**
			NOEC	100
Aquatic algal inhibition, *S. subspicatus* (Report No. SPL 282/594)	Methomyl	72-hour	EC_{50}	**>100**
			NOEC	100

Microcosm or mesocosm tests
None

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

End points in bold are those used in risk assessment.

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
0.45 x 2	Late grapes and listed tall vegetables	Fish	Acute	3	**50.8**	100
		Aquatic invert.			**1.37**	100
		Fish	Chronic		**5.9**	10
		Aquatic invert.			**0.129**	10
		Algae			>8064	10
0.45 x 2	Late grapes and listed tall vegetables	Fish	Acute	50	4200	100
		Aquatic invert.			113	100
		Fish	Chronic		487	10
		Aquatic invert.			10.7	10
		Algae			>666667	10

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
0.45 x 2	Listed low vegetables	Fish	Acute	1	151	100
		Aquatic invert.			**4.1**	100
		Fish	Chronic		17.5	10
		Aquatic invert.			**0.38**	10
		Algae			24096	10
		Fish	Acute	30	4200	100
		Aquatic invert.			113	100
		Fish	Chronic		487	10
		Aquatic invert.			10.7	10
		Algae			>666667	10

Bioconcentration

Bioconcentration factor (BCF) ‡	log Pow = 0.09 at 25°C << log Pow ≥3 (Report No. AMR-1234-88)
Annex VI Trigger:for the bioconcentration factor	None
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 ‡	Methomyl: 48-hour LD_{50} = 0.28 µg/bee (Report No. DuPont-2738)
	Methomyl 20SL: 48-hour LD_{50} = 0.20 µg a.s./bee (Report No. DuPont-2739)
Acute contact toxicity ‡	Methomyl: 48-hour LD_{50} = 0.16 µg/bee (Report No. DuPont-2738)
	Methomyl 20SL: 48-hour LD_{50} = 0.17 µg a.s./bee (Report No. DuPont-2739)

‡ 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				
0.45 kg a.s./ha (methomyl; Report No. DuPont-2738)	Grapes, & listed fruiting vegetables	Oral	1,607	>50
0.45 kg a.s./ha (methomyl; Report No. DuPont-2738)		Contact	2,813	>50
0.45 kg a.s./ha (Methomyl 20SL; Report No. DuPont-2739)		Oral	2,250	>50
0.45 kg a.s./ha (Methomyl 20SL; Report No. DuPont-2739)		Contact	2,647	>50

Field or semi-field tests
Semi-field test: Methomyl 20SL was applied at 450-g a.s./ha to *Phacelia tanacetiflora* and effects on foraging honey bees exposed to spray deposits 2, 6, and 11 days after treatment were recorded. The report concluded that there was no significant effect on mortality when residues were aged for over 2 days. However, the results need to be treated with caution since effects were greater for residues aged for 6 days than those aged for 2 or 11 days. No adverse effects on behaviour, flight activity or incidence of abnormal development were observed (Report No. DuPont-4446). Semi-field: In a similar trial bees were exposed to spray deposits 1, 5, and 10 days after treatment. The report stated that Methomyl 20SL applied at 450-g a.s./ha to apple trees had temporary harmful effects on honey bees, if exposed 1 day after treatment and that this effect persisted for 2 days. However, similar effects were observed from residues aged for 10 days and it was considered that this statement was not supported. Most mortality occurred in the first 2 days of the evaluation period irrespective of the ageing period of the residues thus making results difficult to interpret. No abnormal behaviour and no incidence for abnormal development of the bee brood was observed, due to Methomyl 20SL (Report No. DuPont-5470). On the basis of the information submitted it was considered that there was a potential risk to bees. The information from the aged residue trials was considered to be of only limited use. Member States need to consider appropriate risk management measures for bees.

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

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests ‡						
Tier 1 (glass) – dose response (Report No. DuPont-2668)	*Typhlodromus pyri* – protonymphys	Methomyl 20SL	1, 3, 9, 27, and 81 g/ha	7-day LR_{30} LR_{50}	9.1 g/ha 12.8 g/ha	30%
Tier 2 - extended dose/response (Report No. DuPont-3766)	*Typhlodromus pyri* - protonymphys	Methomyl 20SL	6.25, 12.5, 25, 50, and 100 g/ha	7-day LR_{25} LR_{50}	22.1 g/ha 34.5 g/ha	30%
Tier 2 - field-aged residues (Report No. DuPont-4427)	*Typhlodromus pyri* - protonymphys	Methomyl 20SL	22.5, 33.75, and 450 g/ha	7-day mortality (%) at 33.75 g/ha fresh residues	5.4%	30%
				7-day mortality at 450 g/ha 7-day aged deposits	3.3%	30%
Tier 1 (glass) – dose response (Report No. DuPont-2669)	*Aphidius rhopalosiphi* - adults	Methomyl 20SL	0.006, 0.019, 0.056, 0.167, 0.500 g/ha	48-hr LR_{30} LR_{50}	0.20 g/ha 0.25 g/ha	30%
Tier 2 - dose/response (Report No. DuPont-3764)	*Aphidius rhopalosiphi* - adults	Methomyl 20SL	1, 3, 9, 27, 81 g/ha	48-hr LR_{25} LR_{50} reproduction	8.33 g/ha 14.7 g/ha 35% at 27 g/ha	30%
Tier 2 - extended field-aged residues (Report No. DuPont-2563)	*Aphidius rhopalosiphi* - adults	Methomyl 20SL	1.25 kg/ha	14-day field-aged-residue: mortality (%) 14-day reproduction (result from 1520 g/ha)	2.8% 27.8%	30%

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Tier 1 – spraying over mummified aphids (DuPont-4630)	*Aphidius rhopalosiphi* – protected life stage	Methomyl 20SL	450 g/ha	7-day mortality (%) at 450 g/ha emergence (% decrease) at 450 g/ha	6.81% 3.93%	30%
Tier 2 – field-aged spray deposits on natural soil (Report No. DuPont-3337)	*Poecilus cupreus* - adults	Methomyl 20SL	720 g/ha	1-day field aged residue: mortality, and food consumption (%)	0%, -2.6%	30%
Tier 2 – extended field-aged residues (DuPont-2562)	*Chrysoperla carnea* -larvae	Methomyl 20SL	1250 g/ha	7-day field-aged spray deposits: mortality and reproduction (%)	Mortality 22.2%; Reproduction: 11.5%	30%
Tier 2 lab. Aged residues (Du Pont 3336)	*Aleochara bilineata*	Methomyl 20SL	720 g/ha	1-day aged residues: mortality and reproduction	21.3% 5.3%	30%
Tier 2-extended field aged residues (Du Pont 5514)	*Orius laevigatus*	Methomyl 20SL	450 g/ha	5-day aged residues mortality: reproductive reduction	 29% 9%	30%

Field or semi-field tests
<u>Field tests:</u> Methomyl 20SL applied twice at an interval of 14 days at a rate of 2250 mL/ha (i.e., 450-g methomyl/ha) to grapevine in the field resulted in a maximum of 64% reduction in the population of *Typhlodromus pyri* 28 days after the 2nd application. The population reduction was below 50% (37%) at 81 days after the 2nd application of Methomyl 20SL (Report No. DuPont-3883). Methomyl 20SL applied twice at an interval of 14 days at a rate of 2250 mL/ha (i.e., 450-g methomyl/ha) to grapevine in the field resulted in a maximum effect of 71% reduction compared to controls 28 days after the 2nd application on a mixed population off predatory mites. The population reduction was below 50% (34%) at 338 days after the 2nd application of Methomyl 20SL (Report No. DuPont-4327). Methomyl 20SL applied twice at an interval of 13 days at a rate of 2250 mL/ha (i.e.,

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

450-g methomyl/ha) to grapevine in the field had a maximum effect of 93% reduction compared to controls observed 56 days after the 2nd application on a mixed population off predatory mites. The population reduction was below 50% (23%) at 371 days after the 2nd application of Methomyl 20SL (Report No. DuPont-4326). Methomyl 20SL applied twice at an interval of 14 days at a rate of 2250 mL/ha (i.e., 450-g methomyl/ha) to a mixed predatory mite population had a maximum effect of 87% reduction compared to controls at 27 days after the 2nd application. The population reduction was below 50% (25%) at 56 days after the 2nd application of Methomyl 20SL (Report No. DuPont-5469). Methomyl 20SL applied twice at an interval of 14 days at a rate of 2250 mL/ha (i.e., 450-g methomyl/ha) to grapevine in the field had a maximum effect of 98.7% reduction compared to controls on *Typhlodromus pyri* at 27 days after the 2nd application. The population reduction was below 50% (36%) at 83 days after the 2nd application of Methomyl 20SL (Report No. DuPont-5659). Methomyl 20SL applied at a potential drift rate of 22.5-g methomyl/ha to grapevines in the field had no statistically significant effects on *Typhlodromus pyri* on day 8 (-5%) after application (Report No. 4330). Methomyl 20SL applied at a potential drift rate of 33.75-g methomyl/ha to grapevines in the field had no statistically significant effects on *Typhlodromus pyri* on day 8 (9%) and on day 27 (22%) after application(Report No. DuPont-4329).

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

Acute toxicity ‡	Methomyl: LC_{50} = 19 mg/kg soil dry weight (Report No. DuPont-3926)
Reproductive toxicity ‡	Methomyl 20SL: NOEL = 7.5 mg formulation /kg artificial soil (1.5 mg a.s./kg) (Report No. DuPont-5503)

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
0.45 kg/ha x 2	Listed fruiting vegetables (BBCH 20 onwards)	Acute	69	10
	Early grape (BBCH 50 onwards)		51.8	10

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
0.45 kg/ha x 2	Listed fruiting vegetables (BBCH 20 onwards)	Chronic	**5.5**	5
	Early grapes (BBCH 50 onwards)		**4.1**	5

Using new revised soil PECs as per these endpoints.

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

Nitrogen mineralization ‡	Methomyl 20SL: No significant effect (<25% effect) after 28 days at a rate equivalent to 4.5 kg a.s./ha. (Report No. DuPont-4113)
Carbon mineralization ‡	Methomyl 20SL: No significant effect (<25% effect) after 28 days at a rate equivalent to 4.5 kg a.s./ha. (Report No. DuPont-4113)

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N;	Harmful
	R50/R53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment

‡ 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