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

thiodicarb

finalised: 14 December 2005

(version of 11 January 2006 with minor editorial changes)

SUMMARY

Thiodicarb 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 thiodicarb in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 19 January 2004. Following a quality check on the DAR, the peer review was initiated on 13 February 2004 by dispatching the DAR for consultation of the Member States and the sole applicant Bayer CropScience S.A. (notification and submission made by Aventis CropScience prior to merger to form Bayer CropScience). Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting in September 2004. 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 January – March 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 30 September 2005 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 and molluscicide as proposed by the applicant which comprises foliar spraying to control chewing and sucking insects in table and wine grapes and spreading baits to control slugs and snails in cereals. The application rates are 0.375 kg and 0.2 kg thiodicarb per hectare, respectively. Thiodicarb can be used only as insecticide and molluscicide.
The representative formulated products for the evaluation were "Larvin" and "Skipper", a suspension concentrate (SC) and a granular bait (GB), respectively.

[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 method 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.

Thiodicarb is rapidly and extensively absorbed, via gastrointestinal tract in rats (>70%, based on excretion data) and distributed. Excretion occurs primarily as volatile components (acetonitrile, CO_2) in expired air (about 40%) and in urine (about 30%). Less than 10% is excreted in faeces. The acute toxicity is high, (oral LD_{50} 59 mg/kg bw) as well as during inhalatory exposure (LC_{50} 0.81 mg/L air). Acute dermal LD_{50} is greater than 2000 mg/kg bw. It is not a skin or an eye irritant but is a skin sensitizer (Magnusson and Kligman test). Classification for acute toxicity is needed and the proposed risk phrases are: T; R23/R25 (Toxic by inhalation and if swallowed)" and R43 "May cause sensitization by skin contact". Repeated exposures resulted in decreased body weight and food consumption, alterations in haematological parameters, haemolytic anemia, haemosiderosis and extramedullary haematopoiesis, as well as signs of cholinergic effects. The relevant oral NOAEL for short term exposures is 5 mg/kg bw/day. The NOAELs for chronic toxicity in rats is 3 mg/kg bw/day.
Overall, thiodicarb does not show genotoxic or carcinogenic potential. The parental and reproductive NOAELs for thiodicarb are 7 mg/kg bw/day based on significantly reduced body weights in adults and pups and reduced pup viability at 15 mg/kg bw/day. Due to the increased mortality of pups at dose levels which is not associated with marked maternal toxicity, classification as Cat. 2 and R61 was proposed. A statement was forwarded to ECB (European Chemical Bureau, Ispra).
In teratogenicity studies, the NOAEL for maternal effects in the rat is 1 mg/kg bw/day, based on reduced body weight and clinical signs. The relevant developmental NOAEL is 30 mg/kg bw/day (highest tested dose). In a 90-day study in rats, the NOAEL for neurotoxic effects is 6 mg/kg bw/day, based on the inhibition of brain acetylcholinesterase at 23 mg/kg bw/day and above.
The ADI is 0.01 mg/kg bw/day, from the teratogenicity study in rats with a safety factor of 100. The AOEL is 0.014 mg/kg bw/day, from the two generation study in rats (7 mg/kg bw/day) using a safety factor of 500, due to the severity of reproductive effects. The ARfD is 0.01 mg/kg bw, based on the lowest observed NOAEL of 1 mg/kg bw/day from the teratogenicity study in rats, supported by the LOAEL of 5 mg/kw from the acute neurotoxicity study, with a safety factor of 100**.**
The RMS has provided a risk assessment only for operators exposed to thiodicarb during application of Larvin on grapevines. The exposure estimates is below the AOEL of 0.014 mg/kg bw/day for orchard sprayer activity only when PPE is used (German model); for hand held activities, exposure does not exceed the AOEL even without PPE (German model) or with PPE (UK POEM).
For workers and bystanders the estimated exposure is below the AOEL.

The metabolism of thiodicarb in fruits after foliar application is clearly understood and its main degradation product of toxicological relevance is methomyl. The residue definition proposed for both

monitoring and risk assessment is the sum of thiodicarb and methomyl expressed as methomyl. No other metabolite needs to be considered in the residue definition due to its potential contribution to the toxicological burden. Ultimate degradation products of thiodicarb are acetonitrile and carbon dioxide, the last being reincorporated in endogenous plant materials.
No residues are expected to be present in following crops.
In animal the metabolism of thiodicarb is extensive and no carbamate related compound is present in edible animal commodities. There is no need for defining a residue definition for animal products or to monitor residues resulting from the representative uses of thiodicarb in these products.
In grapes and cereals, supervised residue trials support the establishment of MRLs at 1 and 0.05* mg/kg respectively. In wine the residue transfer is limited and the residue level in wine is not expected to be higher than 50 % of the residue level in raw grapes.
The risk assessment carried out for the representative uses supported by the applicant indicated an acute risk resulting from the consumption of wine and table grapes.

Under dark aerobic conditions in soil methomyl was the only major metabolite of thiodicarb.
Two major metabolites were identified under dark anaerobic conditions S-methyl-*N*-[*N*-methyl-*N*-(methylaminothio) carbamoyloxy] thioacetamidate and acetonitrile. Photolysis may contribute slightly to the environmental degradation of thiodicarb being acetonitrile the only major soil photolysis metabolite.
Thiodicarb is very low to low persistent in soil under aerobic laboratory conditions. Under the same conditions methomyl is low persistent in soils. Whereas not triggered by the directive, field dissipation studies are available for thiodicarb formulated either as water flowable or slow release pellets. Thiodicarb is low to high mobile and methomyl is very high mobile in soil.
In sterile buffer solutions at 25 °C thiodicarb and methomyl degradation are pH dependent. The main product of thiodicarb hydrolysis is methomyl.
Contribution of aqueous photolysis to the environmental degradation of thiodicarb and methomyl is deemed negligible. Thiodicarb is not ready biodegradable.
In water/sediment systems, thiodicarb degrades very fast to methomyl in the water phase (DT_{50} < 1 d). Degradation of methomyl was also fast with half lives between 3.5 to 5 days in the total systems.
PEC sw of the insecticide application is calculated based on spray drift loadings and were found acceptable.
A comprehensive surface water risk assessment, including drainage and runoff routes of entry in surface water, will be necessary to complete the risk assessment of the pellets formulation and the molluscicidal use. RMS decided not to further assess the molluscicide use and the pellet formulation due to the number of data gaps identified at the initial assessment.
The potential leaching of thiodicarb and its metabolite methomyl for the insecticidal use in vines and the molluscicidal use in winter cereals was simulated for the relevant FOCUS gw scenarios. The trigger of 0.1 µg / L was not exceeded for any of the seven scenarios simulated for the insecticidal use (LARVIN) and was exceeded by two of the nine scenarios simulated for the molluscicidal use (SKIPPER). The assessment of the EU representative molluscicidal use may not be considered finalised with respect to the potential for ground water contamination.

For the insecticidal use on vines a new simulation was presented the Addendum 1. This new modelling confirms the results found previously. Monitoring data on cereal cropping areas of UK show occasional breaking of the 0.1 µg / L trigger by methomyl it is not possible to know if the origin of this methomyl is from thiodicarb use or due to the application of products containing methomyl as active substance.
Concentration of thiodicarb in the air compartment and transport through it, is not expected to be significant.

The risk assessment for terrestrial vertebrates was performed in line with the EPPO (1992) risk assessment scheme. The risk to insectivorous birds from the use of 'Larvin' as a foliar spray is considered to be low in terms of acute, short-term and long-term toxicity from the active substance, thiodicarb. With regards to the metabolite, methomyl, the first tier acute toxicity TER highlighted that there was a high risk, which was not seen in either the short-term or long-term assessments. The assessment was refined by using the end point from the short-term dietary study converted to a daily dose instead, as it was proposed to be more appropriate for this scenario. As a result, the TER value was above the Annex VI trigger and acute risk to birds from methomyl was considered to be low. The approach was discussed at the experts' meeting for ecotoxicology (EPCO 17) and it was agreed to await the opinion of the PPR panel for pirimicarb where a similar approach was used. The opinion for pirimicarb was adopted in July 2005[3] and it is proposed by the EFSA that a risk assessment is performed in accordance with the recommendations provided in this opinion. The acute risk to mammals was considered low based on a 1-day dietary study on mice from which the NOEL for mortality was used with a safety factor of 10. The long-term risk to mammals is on the borderline of the Annex VI trigger following refinement based on residue decline in grass.

For the use of the pellet formulation ('Skipper') high acute and long-term risks were identified for birds and mammals. Additionally an acute risk from consumption of methomyl contaminated earthworms was identified. The argumentation and proposals initially presented by the applicant to refine the risk was not considered robust enough by the rapporteur Member State. New data to refine the identified acute and long-term risks to birds and mammals has been provided by the applicant. These data have not been evaluated by the rapporteur Member State and it is therefore at this stage not possible to conclude on the risk from the 'Skipper' formulation.

With regard to the use of 'Larvin' risk mitigation comparable to 40 m buffer zones is required to protect aquatic organisms. With regards to 'Skipper' low risk to aquatic organisms is considered if the product is applied to undrained or peaty soils or to soils represented by Quorndon soils. If 'Skipper' is used on soils more vulnerable to drainage, there is a high potential risk for exposure of surface water via drainage and risk mitigation measures must be considered at Member state level. Additionally contamination of surface water from run-off should be considered. Before the risk assessment for the

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

aquatic environment can be finalised a study on acute toxicity to aquatic gastropods should be conducted and evaluated.

Thiodicarb is toxic to honeybees. However, field data are available showing that after 12 hours residues were non-toxic. For 'Larvin' risk mitigation measures, e.g. applications outside flowering or in the evening are proposed to be considered at Member State level. Due to the timing of the applications for 'Skipper' (autumnal use and applied directly to the ground), the risk to bees from its use is considered low. For non-target arthropods there is a potential for recolonization since residue decline is relatively rapid, effects on mortality and reproduction are below 50% in 5-7 days aged residue studies, and in the case of 'Larvin' less than 50% mortality is expected for the most sensitive species tested at 3 m distance from the treated field. However, the EPCO experts' meeting for ecotoxicology was of the opinion that oral route of exposure had not been sufficiently addressed in the studies and risk mitigation measures for the use of 'Larvin' should therefore be considered at Member State level.

For the use of 'Skipper' the acute risk to earthworms from pellets on the soil surface needs to be addressed. Additionally, a long-term risk to earthworms from the exposure to methomyl was identified. A field study to address the risk is ongoing. Pending the evaluation of new data, the risk assessment for earthworms for the use of 'Skipper' cannot be finalised. The risk to soil microbial processes and to non-target flora is low.

Key words: thiodicarb, methomyl, peer review, risk assessment, pesticide, insecticide and molluscicide

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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. Thiodicarb 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 thiodicarb, hereafter referred to as the draft assessment report, to the EFSA on 19 January 2004. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 13 February 2004 to the Member States and the main applicant Bayer CropScience S.A. as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 28 September 2004 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier was attending this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team at the Federal Office for Consumer Protection and Food Safety (BVL) in Braunschweig in January – March 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 30 September 2005 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. 1-2 of 29 October 2004)
- 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 30 September 2005)

Given the importance of the draft assessment report including its addendum (compiled version of August 2005 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

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

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Thiodicarb is the ISO common name for 3,7,9,13-tetramethyl-5,11-dioxa-2,8,14-trithia-4,7,9,12-tetra-azapentadeca-3,12-diene-6,10-dione (IUPAC).

Thiodicarb belongs to the class of oxime carbamate insecticides such as aldicarb, methomyl and oxamyl. Thiodicarb, as a carbamate, causes metabolic disturbances in insects and warm blooded animals by inhibiting the acetylcholinesterase. It is being assumed that a similar effect occurs in molluscs.

The representative formulated products for the evaluation were "Larvin" and "Skipper", a suspension concentrate (SC) and a granular bait (GB), respectively.

The evaluated representative uses as insecticide and molluscicide comprise foliar spraying to control chewing and sucking insects in table and wine grapes and spreading baits to control slugs and snails

in cereals. The application rates are 0.375 kg and 0.2 kg thiodicarb per hectare, respectively. Thiodicarb can be used only as insecticide and molluscicide.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of thiodicarb as manufactured should not be less than 940 g/kg, which is higher than the minimum purity given in the FAO specification 543/TC/S/F (1997) of 920 g/kg. It should be noted that the higher value is based on toxicological concern (see 2.4) and not to the submitted results of current batch analysis.
The technical material contains methomyl, which has to be regarded as relevant impurity. The maximum content in the technical material should not be higher than 5 g/kg (543/TC/S/F (1997).

The content of thiodicarb in the representative formulations are 375 g/L (pure) for the SC and 40 g/kg for the GB. The maximum content of methomyl in the SC-formulation may not be higher 0.5% of the thiodicarb content in the formulation (543/SC/S/F (1997). For the GB formulation no FAO specification exits for the moment.

The assessment of the data package revealed no particular area of concern apart from the fact that the content of methomyl was not analysed during the shelf-life study for the SC formulation to ensure that the maximum content is in accordance with the FAO specification.

The main data regarding the identity of thiodicarb 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 thiodicarb and methomyl in the technical material and in the representative formulation as well as for the determination of the respective impurity 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. thiodicarb and methomyl in food of plant origin, soil, water, air.
The methodology used is HPLC with UV, fluorescence or MS/MS detection A multi-residue method like the Dutch MM1 or the German S19 is not applicable due to the nature of the residues.
According to the proposed classification as T (toxic) an analytical method for the determination of residues in body fluids (blood) and tissues should be provided. However, in the case of thiodicarb, rat metabolism data confirm that no thiodicarb residues are found in blood and that only trace levels of

some metabolites might be observed (see 2.1). Therefore a chemical specific blood method would serve no purpose in confirming exposure. A method for the determination of residues in animal tissues is also not warranted as it has been shown that thiodicarb derived carbamate residues do not transfer to animal matrices. From a toxicological point of view, cholinesterase activity in blood is the best mean to determine overexposure to thiodicarb.
An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.2).

The discussion in the expert meeting on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material, the shelf-life study for the SC formulation and to the enforcement methods.

2. Mammalian toxicology

Thiodicarb was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 18) in February 2005.

2.1 ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Thiodicarb is rapidly and extensively absorbed, via gastrointestinal tract in rats (>70%, based on excretion data).
It is widely distributed into most tissues including brain. No accumulation is evident except for the red blood cells and the amount of residues is low after 24 hours. The majority is cleared within 24 hours after the administration in rats.
Metabolism starts with hydrolysis to methomyl (methomyl is an anticholinesterase agent as well). In vivo it is further metabolised to acetonitrile, CO2 and low molecular weight polar compounds.
Excretion occurs primarily as volatile components (acetonitrile, CO2) in expired air (about 40%) and in urine (about 30%). Less than 10% is excreted in faeces.

2.2 ACUTE TOXICITY

The acute toxicity is high, (oral LD_{50} 59 mg/kg bw) as well as during inhalatory exposure (LC_{50} 0.81 mg/L air). Acute dermal LD_{50} is greater than 2000 mg/kg bw. It is not a skin or an eye irritant but is a skin sensitizer (Magnusson and Kligman test).
Classification for acute toxicity is needed and the proposed risk phrases are: T; R23/R25 (Toxic by inhalation and if swallowed) and R43 (May cause sensitization by skin contact).

2.3 SHORT TERM TOXICITY

Repeated exposures to thiodicarb resulted in decreased body weight and food consumption, alterations in haematological parameters, haemolytic anemia, haemosiderosis and extramedullary haematopoiesis, as well as signs of cholinergic effects. The relevant oral NOAEL is 5 mg/kg bw/day from the 6-month and the 1-year study in dog.

A MS proposed to classify thiodicarb as R48, due to the haemolytic anemia seen both in short and long term studies. The experts agreed that R48 is not justified, since effects are present only at dose levels at which significant cholinesterase inhibition occurs and no severe dysfunctions are registered. The final decision is up to ECB (European Chemical Bureau, Ispra).

All the repeated dose dermal studies submitted failed in determining a NOAEL. However, the whole picture indicates that thiodicarb should be less toxic via dermal route.

A repeated inhalation study produced cholinergic signs at 0.005 mg/L and above, (corresponding to a systemic dose of approximately 1.5 mg/kg bw/day), indicating a high toxicity via inhalation. Thus, a classification for toxicity during repeated inhalation exposure might be warranted. Final decision is up to ECB.

2.4 GENOTOXICITY

In the DAR the genotoxic properties of thiodicarb were studied in a battery of tests consisting of nine *in vitro* studies and three *in vivo* studies. The gene mutation assay with mouse lymphoma cells gave positive results, as well as the mitotic gene conversion assay in some concentrations. The three *in vivo* studies showed negative results. The experts agreed that the data package on genotoxicity with the technical material was complete. Differences among purities of technical materials in different tests were noticed (minimum purity of the technical material: 94%): the UDS was performed with technical material 95.4% pure, while the micronucleus and the dominant lethal test were conducted with a >99% pure thiodicarb. The 3 *in vitro* studies were performed with a technical material with 91.5% purity. Even with an additional Ames test using the correct minimum purity material, a positive result would not affect the overall picture, since the UDS test is negative. Thus, the experts concluded that there is no genotoxic potential for thiodicarb and no new studies are required.

2.5 LONG TERM TOXICITY

The long term toxicity and carcinogenic potential of thiodicarb were assessed in 2 long term studies in rats and 2 in mice.

Signs of cholinergic toxicity were not seen consistently in any of the chronic toxicity studies performed with thiodicarb. Inhibition of plasma and erythrocyte activities varied pending on the animal fasting/non fasting conditions. Brain cholinesterase was not inhibited in a statistically significant way throughout the studies. Effects other than cholinesterase inhibition consisted in reduction of body weight and food consumption, macrocytic/haemolytic anemia and splenic lesions. The NOAELs in rats is 3 mg/kg bw/day and in mice 5 mg/kg bw/day.

A MS proposed to classify thiodicarb as R48, due to the haemolytic anemia seen both in short and long term studies but it was not agreed on by the experts (see 2.3).

In mice, a statistically significant increase in adenoma and carcinoma of the liver was recorded. The occurrence of these tumours was considered to be of no relevance to human risk assessment because the dose at which the tumours occurred greatly exceeded the maximum tolerated dose.

In a rat study, the overall incidence of benign and malignant tumours was lower than controls in the top dose group. Incidence of thyroid carcinomas in females was slightly above the historical control

range, even of no statistical significance. Top dose males showed also interstitial cell adenoma with testicular atrophy. Nevertheless, a clear threshold for tumours is 12 mg/kg bw/day.
Thus, the overall conclusion is that thiodicarb does not show carcinogenic potential.

2.6 REPRODUCTIVE TOXICITY

One multigeneration study in the rat in order to determine the reproductive effects of thiodicarb is presented in the DAR. The parental NOAEL was 7 mg/kg bw/day based on significantly reduced body weights in adults and pups at 15 mg/kg bw/day. The relevant NOAEL for reproduction is 7 mg/kg bw/day as well, based on significantly reduced pup viability at 15 mg/kg bw/day. In this study, pups were found with no milk in the stomach. Therefore, some MS proposed the classification R64. Neither thiodicarb nor its metabolites were identified in the milk. No correlation was found between dead pups and the number of pups with no milk in the stomach. However, due to the increased mortality of pups at dose levels which are not associated with marked maternal toxicity (the effects in offspring are apparently related to maternal exposure). Therefore, a classification as Cat. 2 and R61 was proposed instead by the experts. A statement was forwarded to ECB (European Chemical Bureau, Ispra).
The NOAEL for maternal effects in the rat is 1 mg/kg bw/day, based on reduced body weight and clinical signs. The relevant developmental NOAEL is from the rat which is 30 mg/kg bw/day (highest tested dose). **Classification for reproductive effects is needed and the proposed risk phrase is Cat. 2, R61 "May cause harm to the unborn child".**

2.7 NEUROTOXICITY

In a single neurotoxicity study in rats, no NOAEL was established, due to the occurrence of clinical signs even at the lowest dose tested (5 mg/kg bw). In a 90-day study in rats, the NOAEL is 6 mg/kg bw/day, based on the inhibition of brain acetylcholinesterase at 23 mg/kg bw/day and above.

2.8 FURTHER STUDIES

Acute toxicity studies on metabolites

The main plant metabolite of thiodicarb is methomyl, which is toxic (oral LD_{50} 32 mg/kg bw).
ADI and ARfD of 0.0025 mg/kg/bw/day were agreed on during the EPCO experts' meeting 33.

2.9 MEDICAL DATA

No adverse work-related health effects were reported for plant personnel so far. No reports of clinical cases or poisonings, except for suicide attempts, have been submitted.

2.10 ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) and ACUTE REFERENCE DOSE (ARfD)

ADI

The meeting agreed on an **ADI of 0.01 mg/kg bw/day,** based on the lowest observed NOAEL of 1 mg/kg bw/day from the teratogenicity study in rats, with a **safety factor of 100.**

AOEL

Initially, the RMS proposed an AOEL of 0.03 mg/kg bw/day. However, the meeting agreed on an **AOEL of 0.014 mg/kg bw/day,** based on the NOAEL from the two generation study in rats (7 mg/kg bw/day) using a **safety factor of 500.** An additional safety factor of 5 is added**,** due to the severity of reproductive effects (classification Repro Cat 2 – R61 proposed).

ARfD

The meeting agreed on an **ARfD of 0.01 mg/kg bw,** based on the lowest observed NOAEL of 1 mg/kg bw/day from the teratogenicity study in rats, supported by the LOAEL of 5 mg/kw bw/day from the acute neurotoxicity study, with a safety factor of 100**.**

2.11 DERMAL ABSORPTION

In the DAR the dermal absorption for Larvin SC and Skipper was proposed to be 20% and 10%, respectively, both for diluted and concentrate formulation, based on physical properties and relative toxicity via oral and dermal route. However, many MS commented the proposal of the RMS and considered a default value of 100% as more appropriate. Therefore, the applicant performed and submitted a new comparative *in vitro* dermal absorption study in human and rat skin with Larvin, which is summarised in the Addendum. The dermal absorption values of 0.15% for the concentrate, 1% for dilutions up to 1:220 and 3% for greater dilutions, were agreed by the experts.

2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection products are:
Larvin is a SC formulation, containing 375 g/kg of thiodicarb for use on grapes. Skipper is a granular bait, containing 40 g/kg of thiodicarb for use on wheat, triticale, rye, oats and barley.
The RMS has provided an addendum (Aug 2005) with new calculations, due to revised dermal absorption values and AOEL, only for the use on grapevines (Larvin).

EFSA NOTE: no recalculations are provided for the other uses which thus must remain an open point.

Operator exposure

LARVIN

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

Model	Method	No PPE	With PPE*
German	Orchard sprayer	112	21
	Hand held sprayer	71	-

Model	Method	No PPE	With PPE*
UK POEM	Orchard sprayer	177	127
	Hand held sprayer	160	73

*PPE (personal protective equipment): for the German model gloves during mixing/loading and application and coveralls during application; for UK POEM gloves during mixing/loading and application

The exposure estimate is below the AOEL of 0.014 mg/kg bw/day for orchard sprayer activity only when PPE is used (German model); for hand held activities, exposure does not exceed the AOEL even without PPE (German model) or with PPE (UK POEM).

SKIPPER

New calculations have to be provided by the RMS

Worker exposure

The worker exposure relating to Larvin use is expected to be below the AOEL (16%).
No data available for Skipper.

Bystander exposure

The bystander exposure relating to Larvin use is expected to be below the AOEL (5%).
No data available for Skipper.

3. Residues

Thiodicarb was discussed at the EPCO experts' meeting for residues (EPCO 19) in February 2005.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. Primary crops

The metabolism of thiodicarb was investigated in tomatoes under experimental conditions representative of the use in grapes. Thiodicarb is stable on the surface of the fruits, but degrades rapidly when coming in contact with plant enzymes. Major terminal residues are thiodicarb and methomyl. Methomyl oxime and methomyl methylol are further degradation products but occurring at lower levels. Carbon dioxide and acetonitrile are the ultimate degradation products which are eliminated as gases or reincorporated into natural products.
Further metabolism studies were conducted on cotton, soybean, maize and wheat under stem injection or topical applications. Although, given the time these studies were performed, only TLC was used as identification technique, a similar metabolic pathway as in tomatoes was observed. The expert meeting (EPCO 19) recommended that a metabolism study on cereals should be requested as the representative use supported by the manufacturer on theses crops (application of granules to the soil) is not covered by the available metabolism studies.

The residue definition for both monitoring and risk assessment is proposed to be the sum of thiodicarb and methomyl, expressed as methomyl. The need for including methomyl oxime in the residue definition for risk assessment was discussed during the experts' meetings (EPCO 18 and 19) but it was concluded that this compound does not represent a significant toxicological concern in comparison with thiodicarb and methomyl.

A sufficient number of residue trials were submitted in support of the representative uses in cereals and grapes. The methods of analysis used in these trials measured thiodicarb, methomyl and methomyl oxime as the oxime. Although the oxime is not covered by the residue definition, its contribution to the total residue is very low, as indicated in the metabolism studies, therefore the results can be considered as fully acceptable to be used in risk assessment and in MRL setting.

Supervised residue trials were conducted on barley and wheat in Southern and Northern Europe. Due to the early stage of application of thiodicarb in cereals no difference in the residue behaviour is expected between the various cereals and therefore, all the results can be considered as a whole. Except in one sample of barley straw where positive residues were found (0.052 mg/kg), residues in all grain and other straw samples were below the LOQ (Limit of Quantification) of 0.04 or 0.05 mg/kg. This evaluation of the cereal data base is to be considered as provisional and is under the restriction of the results of the requested metabolism study for confirmation of the validity of the residue definition in cereals.

Supervised residue trials were conducted in grapes in Southern and Northern region. Results are quite similar between both region and support an MRL of 1 mg/kg for table and wine grapes.

The validity of the information provided by the supervised residue trials is supported by storage stability studies of residues of thiodicarb and methomyl indicating that these residues are stable in tomato paste and puree for up to 9 months under storage at temperature between 0 and -10 °C. These tomato matrices can be considered as a worst case covering uses in grapes and cereals.

Studies are available on the effect of processing on the nature and the level of residues in processed commodities. Under conditions simulating pasteurisation, boiling, baking, brewing and pasteurisation, thiodicarb degrades to methomyl and further to methomyl oxime. Other minor compounds are formed of which only one could be tentatively identified as acetonitrile. The extent of degradation of thiodicarb is the most important under sterilisation conditions but even in this case thiodicarb and methomyl remain the major contributors to the total residues. This suggests that there is no need for a specific residue definition to be applied to processed commodities.

Four processing studies were submitted about the transfer of residues from grapes to wine. The results of these studies are rather dispersed but demonstrate that the production of wine leads to at least a 50 % reduction of the residue level.

3.1.2. Succeeding and rotational crops

Rotational crop studies were conducted on mustard, radish and wheat. These studies indicate that residues of methomyl and methomyl oxime can be present at low levels (around 0.01 mg/kg) in crops planted 30 days after application of thiodicarb. Under normal practice, considering that grapevines are perennial crops and that the use on cereals is made at sowing or at early stage of the crop, it is unlikely that residues could be found in following crops.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Metabolism studies were conducted with laying hens and lactating goats. These studies indicate that although thiodicarb may survive some period in the digestive track of animals, once it is absorbed into the bloodstream it is almost instantly hydrolysed to methomyl which is itself quickly metabolised to its oxime and further to carbon dioxide. An important fraction of the administered radioactivity is expired as CO_2 and acetonitrile. Acetonitrile and acetamide are the only compounds to be present in edible animal commodities beside other natural compounds resulting from the incorporation of CO_2 in the animal metabolism. Thiodicarb or related carbamate/oxime metabolites were never found in these tissues.

Considering the information provided by these metabolism studies, and taking into account the very low potential intake of thiodicarb and methomyl by domestic animals resulting from the representative uses, no livestock feeding study needs to be submitted and no residues definition needs to be proposed.

3.3. CONSUMER RISK ASSESSMENT

Consideration was given during the expert meeting (EPCO 19) on the critical toxicological end points to be used for risk assessment of residues resulting from the use of thiodicarb. As residues in the supervised trials were measured as total residues, it is not possible to estimate the respective contribution of thiodicarb and methomyl. Therefore it was decided that the end points of the most toxic of these 2 compounds should be used, considering that effects of methomyl and thiodicarb are the same and cumulative. As indicated under point 2.10 the ADI and the ARfD of thiodicarb have been set at 0.01 mg/kg bw/d. At this stage of the peer review however, the ADI and the ARfD of methomyl have not yet been formally adopted. During the expert meeting on toxicology (EPCO 33), the ADI and the ARfD of methomyl were established at 0.0025 mg/kg bw/d. Therefore the ADI and the ARfD of methomyl are used in the framework of these conclusions. This means that the calculated acute and chronic intakes, when calculated as % of the ADI and ARfD in the DAR, have to be multiplied by a factor 4 to lead to values mentioned in the list of endpoints in appendix I of these conclusions.

The chronic dietary risk assessment has been carried out using the International (National) Estimated Daily Intake (I(N)EDI) calculation model of WHO using the WHO European typical diet for adult consumers and the national diet of UK for high consumers in infants and toddlers populations (97.5th percentile of the distribution). Residues in table and wine grapes, as well as in cereals were assumed to be at the level of the respective STMR (Supervised Trials Median Residue). For wine, the relevant transfer factor has been applied to the STMR of the raw commodity. The calculations made for both diets lead to NEDI values up to 80% of the ADI of methomyl.

On acute level, potential short term exposures were calculated using the WHO methodology and the large portion consumption data reported for various population groups of UK. The National Estimated Short Term Intakes were calculated to be below the ARfD of methomyl for cereals, in

excess of the ARfD for wine (~ 140 % in adult population) and largely in excess of the ARfD (about 400% and 1600% for adults and toddlers respectively) for table grapes. A potential risk for consumers has therefore been identified for the representative use in grapes.

3.4. PROPOSED MRLS

The following MRLs are supported by the results of supervised residue trials for the representative uses and their analysis according to statistical tools recommended by current guidelines:
Table and wine grapes: 1 mg/kg
Cereals: 0.05* mg/kg (* indicating that the MRL is set at the level of the limit of quantification of the method of analysis).
However, as far as table and wine grapes are concerned, an acute risk for the consumers has been identified.

4. Environmental fate and behaviour

4.1. FATE AND BEHAVIOUR IN SOIL

Thiodicarb was discussed at the EPCO experts' meeting for Fate and Behaviour in the environment (EPCO 16) in January - February 2005. Addendum 1 (January 2005) was discussed in this experts' meeting. In this meeting the RMS indicated that due to some problems in the ecotoxicological risk assessment of the molluscicidal product (Skipper) has decided not to further assess this use. Therefore, it is labelled grey in the table of representative uses.

4.1.1. Route of degradation in soil

Route and rate of degradation of thiodicarb under dark aerobic conditions at 20 °C or 25 °C was investigated in two separated studies with three soils (20 °C, 40 % MWHC) and one soil (25 °C, 75 % FMC at 1/3 bar) respectively. The four soils covered a range of pH (5.4 – 7.6), clay contents (9.7 % - 27.6 %) and organic matter content (0.5 % - 8.1 %). Degradation in one of the soils was also tested at 10 °C.
Under aerobic conditions in soil **methomyl** (S-methyl N-(methylcarbamoyloxy)thioacetimidate, max 79.8 % AR after 1d) was the only major metabolite of thiodicarb. Another metabolite identified was the minor metabolite methomyl oxime (N-hydroxyethanimidothioic acid methyl ester, max 1.66 % AR after 0.25 d). Unextractable residues accounted for up to 65.6 % AR and CO_2 for 30.2 % AR at the study end.
Degradation under dark anaerobic conditions was investigated in one study with one soil. Two major metabolites were identified in this study **S-methyl-*N*-[*N*-methyl-*N*-(methylaminothio) carbamoyloxy] thioacetamidate** (max 28.2 % AR after 8 min) and **acetonitrile** (max 77.9 % AR after 1 h). Only minor amounts of methomyl or methomyl oxime were identified under anaerobic conditions.
Two soil photolysis studies are available one with thiodicarb and one with its metabolite methomyl. Photolysis may contribute slightly to the environmental degradation of thiodicarb. Acetonitrile was the only major soil photolysis metabolite (max 40 % AR after 30 d, study end).

No new metabolites are found on the available field studies. Degradation of methomyl is significantly enhanced under irradiated conditions.

4.1.2. Persistence of the active substance and their metabolites, degradation or reaction products

Additional to the studies presented under the route sections for thiodicarb, two more studies are available to determine the rate of degradation of methomyl in soil under aerobic conditions at 20 °C. 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.

Thiodicarb is very low to low persistent in soil under aerobic laboratory conditions (DT_{50} = 0.13 – 1.2 d). Under the same conditions methomyl is low persistent in soils (DT_{50} = 4 – 9.9 d). Another study in a sandy loam soil was available in the dossier that show longer halve lives for thiodicarb (DT_{50} = 3.6 d) and methomyl (DT_{50} = 31 d). Whereas the study was considered initially valid by the RMS, 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 RMS in the addendum and discussed in the experts meeting. The meeting agreed that these values should not be use for the EU risk assessment and that the values derived from the dark control of the soil photolysis study could be use as an additional aerobic degradation rate in this case.

Under anaerobic conditions in laboratory degradation of thiodicarb is faster and degradation of methomyl is slightly slower than under aerobic conditions.

Whereas not triggered by the directive, field dissipation studies are available for thiodicarb formulated either as water flowable or slow release pellets. 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 RMS in addendum. 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 methomy the revised half life 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. RMS 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).

The field study with the pellets formulation was used to estimate the release rate of thiodicarb from the pellets under field conditions ($DT_{50\ release}$ = 5.7 d). Acceptability of the release rate was challenged by some comments from MS in the evaluation meeting but was not discussed in the experts meeting because the RMS decided not to further assess the molluscicide use and the pellet formulation due to the number of data gaps identified at the initial assessment.

In the original DAR, PEC soil were calculated for the insecticidal and molluscicidal uses using worst case field half life of thiodicarb and 14 d interval between applications. Only initial PEC soil was calculated for methomyl assuming no degradation between applications. After revision of the field study (Norris, 1991a) new PEC soils were provided by the RMS in the addendum for LARVIN based on worst case laboratory half lives for thiodicarb ($DT_{50\ lab}$ = 1.2 d) and methomyl ($DT_{50\ lab}$ = 15.2 d). However, the soil risk assessment has not been updated and it is based on the values originally calculated by the RMS in the DAR.

4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

Batch adsorption/desorption studies are available for thiodicarb and its metabolites methomyl and methomyl oxime. The results for these studies indicate that thiodicarb is low to high mobile (K_{oc} = 55.2 – 1006 mL / g) and 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.

Aged column leaching studies are available for thiodicarb and methomyl. Thiodicarb study was of limited value because the ageing period lasted far in excess of the DT_{50} of thiodicarb. Major radioactive component in the leachate of the methomyl study 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 thiodicarb and methomyl degradation are pH dependent. Half life for thiodicarb is 0.26 d at pH 9, 30 d at pH 7 and 69 d at pH 5. The main product of thiodicarb hydrolysis is methomyl. Under the same conditions, methomyl is stable at pH 5 and pH 7 but degrades at pH 9 with a DT_{50} = 15.1 d.

Based on the molar extinction coefficient at wavelengths greater than 290 nm, contribution of aqueous photolysis to the environmental degradation of thiodicarb and methomyl may be excluded.

Thiodicarb is not ready biodegradable according the available study.

A study with two dark aerobic water sediment systems incubated at 20 °C is available. Thiodicarb degrades very fast to methomyl in the water phase (DT_{50} < 1 d). Levels of methomyl increase up to 17 % - 50 % AR after one day in the total system and then degraded with a half life between 21 and 29 hours.

Also a two water sediment studies with two dark aerobic systems incubated at 20 °C in each study 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. Degradation of methomyl was also fast with half lives between 3.5 to 5 days in the total systems. Unextractable residues in the sediment reached a maximum of 21 % AR after 14 d declining to 15 % AR at the end of the study (102 d). CO_2 reached a maximum of 46 % AR at the end of the study. Acetonitrile was found in the volatiles trap to a maximum of 27 % AR. Acetonitrile was also the only metabolite that exceeds 10 % AR in the sediment phase. PEC sw of the insecticide application is calculated based on spray drift loadings. Since thiodicarb and its metabolite methomyl are not persistent in soil it is expected that this route of entry to surface water will be dominant over run off and drainflow. However, new surface water

calculations with re-evaluated worst case half lives using non linear regression (thiodicarb $DT_{50\ water}$ = 0.1 d; methomyl $DT_{50\ water}$ = 4.5 d) and a interval between applications of 28 d were presented in the addendum. In this case single application spray drift PEC sw represents the worst case that should be used for the risk assessment.

For the pellets slow release molluscicide application, drain flow PEC sw using MACRO 4.2 were calculated covering winter wheat use in UK. The pertinence of the scenarios simulated for the whole EU is assessed. Whereas this approach does not follow the agreed FOCUS sw scheme, it is useful to show that drainage may play an important role and needs to be fully assessed. Also the uses in southern EU are not covered by this simulations and run off has not been considered. A comprehensive surface water risk assessment, including drainage and runoff routes of entry in surface water, will be necessary to complete the risk assessment of the pellets formulation and the molluscicidal use. This was not further discussed in the experts meeting since RMS decided not to further assess this use due to the number of data gaps already identified in the initial assessment.

4.2.2. Potential for ground water contamination of the active substance their metabolites, degradation or reaction products

The potential leaching of thiodicarb and its metabolite methomyl for the insecticidal use in vines and the molluscicidal use in winter cereals was simulated with FOCUS PRZM 2.4.1 for the relevant FOCUS gw scenarios. RMS repeated the modelling exercise adjusting some of the input parameters. Mean half life from laboratory experiments was used to describe the degradation of thiodicarb (DT_{50} = 0.68 d) and methomyl (DT_{50} = 7.38 d). The trigger of 0.1 µg / L was not exceeded for any of the seven scenarios simulated for the insecticidal use and was exceeded by two of the nine scenarios simulated for the molluscicidal use. RMS decided not to further assess this use due to the number of data gaps already identified in the initial assessment therefore the results and in particular the release rate form the pellets employed in the simulation was not discussed by the experts' meeting. As consequence, the assessment of the EU representative molluscicidal use may not be considered finalised with respect to the potential for ground water contamination.

For the insecticidal use on vines a new simulation was presented by the notifier and summarized in the addendum 1 by the RMS, using FOCUS PEARL v.2.2.2 and FOCUS PRZM v.2.4.1. Re-evaluated and normalized degradation parameters (thiodicarb: DT_{50} = 0.39 d; methomyl: DT_{50} = 5.81 d) and an application interval of 28 d are used in this new modelling.

Monitoring data on cereal cropping areas of UK show occasional breaking of the 0.1 µg / L trigger by methomyl it is not possible to know if the origin of this methomyl is from thiodicarb use or due to the application of products containing methomyl as active substance.

4.3. FATE AND BEHAVIOUR IN AIR

Concentration of thiodicarb in the air compartment and transport through it is not expected to be significant. Thiodicarb does not volatilise appreciably from soil surfaces and according Atkinson calculations it may be photochemically degraded in the atmosphere with a half life of 9.7 h.

5. Ecotoxicology

Thiodicarb was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 17) in January - February 2005. Only issues related to the formulation 'Larvin' was discussed since further data related to the formulation 'Skipper' that had been submitted by the applicant was not evaluated by the Rapporteur.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk to terrestrial vertebrates was assessed based on the use of thiodicarb in table and wine grapes as a foliar spray, 'Larvin', and in cereals as a pellet formulation, 'Skipper'. For the use in grapes a small insectivorous bird and an herbivorous mammal were considered as relevant. Insects were assumed to be exposed to a single application of 0.375 kg a.s./ha, while for herbivorous mammals two applications were considered. For the use of 'Skipper' broadcast application was considered as a worst case that would cover also a first application as admixture with the seeds before drilling. Since no information on how many pellets would be left on the soil surface as a result of admixture application is available, the Rapporteur considered it currently impossible to quantify the potential risk mitigation that would result from admixture application. The Rapporteur proposed that this could be considered at Member State level if the necessary information is available.

For birds, acute, dietary and reproductive toxicity studies were available for thiodicarb and the metabolite methomyl. For mammals, it was assumed that thiodicarb is so rapidly metabolised to methomyl that the risk assessment for thiodicarb also covers the risk from methomyl exposure.

The Rapporteur estimated theoretical exposure (ETE) in line with the EPPO (1992) risk assessment scheme since the Guidance Document on Risk Assessment for Birds and Mammals (SANCO/4145/2000) was not finalised at the time of dossier submission. A conversion factor of 2.4 was used to convert values from dry weight to fresh weight for comparison with the acute toxicity study in the case of 'Larvin'. For the acute assessment for 'Skipper' food intake was not converted to fresh weight since it was considered that acute risk would occur only when the pellets are dry. For short-term and long-term assessments a direct comparison between toxicity endpoint as concentration in the diet and the ETE value was done. The risk assessments were discussed at the experts' meeting and several Member States pointed out that a risk assessment according to SANCO/4145/2000 would have been preferred since some TER values are close to the Annex VI triggers. The EFSA agrees to this opinion.

For the use in grapes, acute, short-term and long-term TER values calculated according to the EPPO-scheme for insectivorous birds are above the Annex VI trigger values for thiodicarb indicating a low risk. For the metabolite methomyl, the acute TER is 3.4, indicating a potential high risk. The applicant argued that the use of the standard acute end point is not relevant due to the fact that thiodicarb and methomyl are rapidly metabolised and the feeding rate of a small bird eating insects is unlikely to result in the consumption of sufficient treated food for a lethal dose to be obtained in a single day. The applicant proposed that the most appropriate end point to be used in determining the

acute risk is the LC_{50} from the 5-day short-term dietary test converted to a daily dose. The Rapporteur considered the proposal acceptable and in line with the 'time quotient > 1' scenario put forward in the 'Report of the SETAC/OECD Workshop on Avian Toxicity Testing' (OECD 1996) and also with the risk assessment conducted for pirimicarb. The Rapporteur recalculated the short-term LC_{50} to daily dose in mg a.s./kg bw/day using food consumption and body weight data in accordance with SANCO/4145/2000. The resulting TER value is 92.3, which is above the Annex trigger of 10 and thus indicates a low risk. The risk assessment was discussed at the experts' meeting and it was decided to await the opinion of the PPR panel for pirimicarb on the 'time quotient >1' approach. The opinion on pirimicarb was adopted in July 2005[4], and it is proposed by the EFSA that a risk assessment is performed in accordance with the guidance provided in this opinion. Since the log Pow is <3 bioaccumulation potential is considered low and no assessment of secondary poisoning is necessary for the foliar use of thiodicarb.

For the product 'Skipper' potential high acute, short-term and long-term risks for birds were identified (TER_a = 0.17, TER_{st} >0.14, TER_{lt} = 0.0125) from direct consumption of pellets. The studies and information available in the original dossier to refine the acute and short-term risk was not considered satisfactory by the Rapporteur. Since the majority of use of thiodicarb pellets will occur during autumn and winter and the dissipation DT_{50} has been estimated to 6 days, the Rapporteur considered exposure during breeding season unlikely for northern Member States. However, this may not be the case in southern Member States. Since further data provided by the applicant was not evaluated by the Rapporteur, the long-term risk to birds from use of 'Skipper' was not discussed at the experts' meeting.

Two studies on residues in earthworms are available, one with a maximum concentration of 18 mg a.s./kg (converted to 16.38 mg methomyl/kg) following application of 5.3 kg product/ha (212 g a,s/ha) and another one with a maximum concentration of 3 mg/kg. The Rapporteur considered the worst case value of 18 mg/kg should be used and based the risk assessment on this value. The acute risk calculated for small birds eating earthworms containing methomyl residues is high (TER =2.1), while the short-term and long-term TER values indicate a low risk. The TER values for thiodicarb indicate a low risk for earthworm-eating birds.

The risk to large herbivorous birds from consumption of thiodicarb or methomyl contaminated vegetation following application of 'Skipper' was calculated based on residue levels in leaves. The risk is considered low, based on TER values well above the Annex VI triggers for acute, short-term and long-term risk.

The first tier acute and long-term risks to herbivorous mammals from the use of thiodicarb as a foliar spray (and therefore from methomyl) were considered high as the TERs are below the relevant Annex VI trigger values (TERs of 2.07 and 2.98, respectively). For insectivorous mammals both the acute

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

and long-term TERs are well above the triggers and hence the risk is considered low. A 1-day mouse feeding study, intended to more closely replicate the natural feeding pattern of small mammals, has been submitted by the applicant to refine the acute/short-term risk from the use of 'Larvin' to herbivorous mammals. The feeding study shows that it is possible for mice to have an intake of thiodicarb relative to their body weight in excess of the gavage LD_{50} without any mortality. The Rapporteur performed the refined acute risk assessment in line with the EPPO scheme as presented in Addendum 1, using both the NOEL of 202 mg a.s./kg bw for mortality and the overall NOAEL of 95 mg a.s./kg bw based on no effects on body weight, clinical signs or food consumption. A deposition of 40% for grapevines at the relevant growth stage was considered in accordance with EU Generic Guidance for FOCUS Groundwater Scenarios. The TER values obtained are 15.3 and 7.2 respectively. The refined risk assessment was discussed at the experts' meeting and it was agreed that in this specific case this approach could be accepted since a NOEL or NOAEL rather than an LD_{50} was being used. Although one of the TERs was below 10 this was based on sublethal effects and not mortality. The meeting agreed that the acute risk was addressed.

A residue study on grass was submitted to refine the long-term risk to herbivorous mammals. The study indicated a rapid decline of thiodicarb residues on grass under European conditions. Worst case DT_{50}s' of 8.1 and 4.95 days was calculated by the applicant and the Rapporteur respectively. Both values were used in the risk assessment. Toxicity values from two relevant multigeneration studies are available in the original DAR (84 and 100 ppm respectively) and both values were used in the refined assessment presented in Addendum 1. Using the DT_{50} of 8.1 days and the NOAEL of 84 ppm a long-term TER of 4.6 was obtained. With the lower DT_{50} the TER is 4.95. The majority of the experts at the EPCO meeting, including EFSA, were of the opinion that since the long-term TER values are close to the trigger, the assessment should have been performed according to the new guidance (SANCO/4145/2000).

With regards to the consumption of pellets ('Skipper'), both the acute and long-term risks were high (TERs of 0.00417 and 0.0025, respectively). Also a high acute risk to small mammals from the consumption of methomyl contaminated earthworms (TER of 3.9) was identified. The acute and long-term risk from consuming contaminated vegetation was low. Further data provided by the Rapporteur to refine the risk has not been evaluated by the Rapporteur.

In conclusion, the risk assessments carried out in line with the EPPO scheme indicates that the risk to birds from the proposed use of 'Larvin' is low, pending the opinion of the PPR panel on the 'time quotient > 1' approach also proposed for pirimicarb. The acute risk to mammals was considered low based on a 1-day dietary study on mice from which the NOEL for mortality was used with a safety factor of 10. The long-term risk to mammals is on the borderline of the Annex VI trigger following refinement based on residue decline in grass. For the use of the pellet formulation ('Skipper') high acute and long-term risks were identified for birds and mammals. Additionally a risk from consumption of earthworms was identified. The applicant has provided new data to refine the identified acute and long-term risks to birds and mammals. These data have not been evaluated by the

Rapporteur and it is therefore at this stage not possible to conclude on the risk from the 'Skipper' formulation.

5.2. RISK TO AQUATIC ORGANISMS

Daphnia magna was the most sensitive of the aquatic organisms tested to technical thiodicarb, with regard to acute toxicity (EC_{50} =0.027 mg/L). The single major metabolite methomyl was of similar toxicity as the parent compound, with an EC_{50} of 0.017 mg/L for *D. magna*. The formulation Larvin was less acutely toxic (LC_{50} = 0.11 mg a.s/L).

An early life stage study with fathead minnow (*Pimephales promelas*) (growth NOEC 0.027 mg/L) and a water spiked reproduction test with *Chironimus riparius* (reproductive NOEC 0.080) are available for thiodicarb, but no valid chronic toxicity study on *Daphnia*. However, since DT_{50} for thiodicarb is 0.1 day no formal long-term risk assessment is required. For methomyl a reproduction study with *Daphnia magna* is available (NOEC 0.0016 mg/L) but no long-term study with fish. The DT_{50} for methomyl is 4.5 days in water and therefore a long-term risk assessment was performed.

For the use of 'Larvin', the maximum predicted environmental concentration of thiodicarb in surface water was calculated based on 8.02% spray drift to a 30 cm static water body at 3 m distances from a single application of 375 g a.s./ha. All first tier TER values were calculated based on initial concentrations. For fish and algae the acute TER values are above the Annex VI trigger indicating a low risk. For *D. magna* a 30 m buffer zone is required to just meet the acute trigger (TER=98). For methomyl the maximum PEC was derived from 2 applications at 375 g a.s./ha and 82nd percentile drift. Risk mitigation comparable to 40 m buffer zones are required to protect aquatic invertebrates (TER = 108). The Rapporteur based the long-term risk assessment for methomyl on the NOEC value for *Daphnia* and the toxicity values for *P. promelas* and *C. riparius* obtained with thiodicarb. Methomyl and thiodicarb was considered of similar toxicity based on the results from the acute studies. However, since no metabolites were found above 10% of applied radioactivity in the water/sediment studies no formal risk assessment for sediment dwelling organisms is required. Risk mitigation measures comparable to 40 m buffer zones are required for 'Larvin' to reach a long-term TER for *Daphnia* which is above the relevant Annex VI trigger (TER = 10.2).

Risks from run-off, drain flow and leaching into ground/surface water have not been assessed for 'Larvin'. The Rapporteur considered the risk from these routes as low for the use of thiodicarb as foliar spray.

For the use of the pellet formulation 'Skipper' no exposure of surface water due to spray drift will occur, and it was considered that drain flow and groundwater contamination would be the main routes of exposure. However, only the risk to methomyl was considered necessary to assess. The maximum PEC modelled using MACRO 4.2 was 33.5 µg methomyl/L (for details see section 4.2.1). Modelling was also used to see how often the critical concentration of 0.16 µg/L (NOEC of 1.6 µg methomyl/L / 10) was exceeded in different types of soils. The results show that low risk is expected to aquatic

organisms from undrained or peaty soils. However, for soils more vulnerable to drainage a high potential risk was identified and risk mitigation measures must be considered at Member State level. No assessment based on run-off was conducted and should be considered to complete the risk assessment.

For two of the nine FOCUS groundwater scenarios the annual year concentrations of methomyl are above 0.1 µg/L and since methomyl is an active substance it must be ensured at Member State level that concentrations do not exceed 0.1 µg/L.

As the bioconcentration factor is 6.3 and the log Pow <2, it is unlikely that thiodicarb or its major metabolite methomyl will bioconcentrate.

Since thiodicarb is used as a molluscicide it was discussed at the experts' meeting whether the risk to gastropod molluscs should be assessed. It was agreed that in this specific case a data requirement for the applicant to conduct an acute study with an aquatic gastropod species should be set. The meeting also agreed that if the acute toxicity to gastropods is less than for Daphnia, no chronic testing will be necessary.

In conclusion, with regard to the use of 'Larvin' risk mitigation comparable to 40 m buffer zones is required to protect aquatic organisms. With regards to 'Skipper' low risk to aquatic organisms is considered if applied to undrained or peaty soils. If 'Skipper' is used on soils that are more vulnerable to drainage a high potential risk was identified and risk mitigation measures must be considered at Member State level. Furthermore, also contamination due to run-off should be considered. Before the risk assessment for the aquatic environment can be finalised a study on acute toxicity to aquatic gastropods should be performed and evaluated.

5.3. RISK TO BEES

'Larvin' is proposed for use on wine and table grapes before and after flowering and may therefore be applied when bees are attracted to the crop to forage on flowering weeds within the crop or on damaged fruit. Bees may be exposed to thiodicarb directly from spray or from residues in the treated crop. The studies available for thiodicarb and 'Larvin' indicate a high acute oral and contact toxicity. The calculated hazard quotients are all above the Annex VI trigger indicating a high risk. A field study and measurements of residue decline in grass was therefore considered. The experts' meeting agreed that the field study covers the risk for bees exposed via contact in sprayed vines and that residue decline is relatively rapid. The residues were non-toxic to bees after 12 hours. However, it was not considered that oral exposure from foraging on flowering weeds was sufficiently covered. Risk mitigation measures were therefore proposed to be set at Member State level.

Due to the timing of the applications for 'Skipper' (autumnal use and applied directly to the ground), there is unlikely to be a risk to bees from its use. As a result, no risk mitigation measures are required.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Laboratory data on toxicity for 'Larvin' and/or methomyl is available for the standard species *Aphidius rhopalosiphi* and *Thyphlodromus pyri* in glass plate tests and extended laboratory tests. Additionally, glass plate tests with the parasitoid *Trichogramma cacoeciae* and the foliage dwelling *Chrysoperla carnea* and *Orius laevigatus*, and extended laboratory tests with the ground dwelling species *Poecilus cupreus* and *Aleochara bilineata* are available. Toxicity of thiodicarb and methomyl was considered comparable. *Aphidius rhopalosiphi* was the most sensitive species. Based on the LR_{50} of 125.8 g a.s./ha and the highest rate without effects of 25.6 g a.s./ha from the extended study, the Rapporteur concluded in Addendum 1 that less than 50% of the population would be expected to be killed at 3 m from the field where exposure was calculated to be 30.1 g a.s./ha (8.02% spray drift). Since total toxic residues were found to decline with a worst case mean DT_{50} of 8.1 days, recolonization from off-field areas was considered possible. The risk to non-target arthropods was discussed at the experts' meeting and the risk was considered as high. There was some concern that the oral route of exposure had not been sufficiently addressed as thiodicarb is systemic, and also the close relationship between target species and some non-target species was of concern. The meeting was of the opinion that risk mitigation measures for the use of 'Larvin' should be considered at Member State level.

For 'Skipper' it is considered that the crop relevant species likely to be exposed are ground dwelling arthropods. The arthropods will be exposed to thiodicarb in the pellet and to thiodicarb and methomyl in the soil. Studies with *Poecilius cupreus* and *Aleochara bilineata* using 'Skipper' or methomyl are available to address the risk. First tier mortality of 77% was observed for *Poecilius*, however when 1-day aged residues of methomyl was used no effects were observed. For *Aleochara* no significant effects were observed in the laboratory study with 'Skipper' or with methomyl in an extended laboratory study when residues were aged for five days. Therefore it was considered that there is a potential for recolonization.

5.5. RISK TO EARTHWOMS

Studies on acute toxicity to earthworms are available for thiodicarb, methomyl and the product 'Larvin', along with chronic toxicity studies on thiodicarb and methomyl (available to the Rapporteur for the methomyl review). A study with a formulation comparable to 'Larvin' shows that the product is not more toxic than the active substance itself. The acute TER values for earthworms are well above the Annex VI trigger for both thiodicarb and the metabolite methomyl from the use of 'Larvin', thus indicating a low acute risk. The long-term TER for thiodicarb is 8.4, hence also the long-term risk is considered low. The DT_{90} for methomyl is between 100 and 365 days, and since the number of applications is less than 3 and the acute toxicity is low, the long-term risk for the metabolite is considered low.

The study provided for the pellet formulation 'Skipper' was not considered appropriate to address the acute risk from pellets on the soil surface and hence a new study is required. Additionally a long-term risk to earthworms from the exposure to methomyl was identified (TER = 2.6) A field study to

address the risk is ongoing. Pending the evaluation of new data, the risk assessment for earthworms for the use of 'Skipper' cannot be finalised.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

The DT_{90} for thiodicarb is less than 100 days and therefore no additional studies on soil macro-organisms are required. For methomyl, the DT_{90} is 144, but since the risk to earthworms, soil microbial processes and non-target soil dwelling arthropods from methomyl when applied as foliar spray is low, the risk to soil non-target macro-organism from use of 'Larvin' is considered low.

From the use of 'Skipper' a potential risk to earthworms has been identified. Pending the evaluation of new studies conducted to address the acute risk from thiodicarb and the long-term risk from methomyl, no conclusion can be drawn on the risk to non-target soil macro-organisms from the use of 'Skipper'.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of technical thiodicarb on soil respiration and nitrogen transformation were tested. No deviations of more than 25% were observed (i.e. no breaching of Annex VI trigger value) at concentrations covering the expected soil concentrations. Hence the risk to soil micro-organisms was considered to be low.

No specific studies are available with the major soil metabolite methomyl. This was discussed at the experts' meeting and it was concluded that peak concentrations of methomyl could be assumed to occur within the duration of the studies with the parent compound. Hence the risk is considered to be low.

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

No effects were observed on 5 crop species, 9 monocotelydon weed species and 10 dicotelydon weed species in standard herbicidal activity screening tests at proposed dose rates for 'Larvin' and 'Skipper'.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

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

6. Residue definitions

Soil

Definitions for risk assessment: thiodicarb and methomyl

Definitions for monitoring: thiodicarb and methomyl

Water

Ground water

Definitions for exposure assessment: thiodicarb and methomyl

Definitions for monitoring: thiodicarb and methomyl

Surface water

Definitions for risk assessment: thiodicarb and methomyl

Definitions for monitoring: thiodicarb and methomyl

Air

Definitions for risk assessment: thiodicarb and methomyl

Definitions for monitoring: thiodicarb and methomyl

Food of plant origin

Definitions for risk assessment: sum of thiodicarb and methomyl expressed as methomyl

Definitions for monitoring: sum of thiodicarb and methomyl expressed as methomyl

Food of animal origin

Definitions for risk assessment: No definition is needed

Definitions for monitoring: No definition is needed

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
thiodicarb	very low to low persistent ($DT_{50\ lab}$ = 0.13 – 1.2 d) moderately persistent under field conditions ($DT_{50\ field}$ = 18 d)	See 5.5, 5.6 and 5.7
methomyl	low to moderate persistent ($DT_{50\ lab}$ = 4 – 9.9 d; $DT_{50\ field}$ = 18 – 43 d)	See 5.5, 5.6 and 5.7
S-methyl-*N*-[*N*-methyl-*N*-(methylaminothio) carbamoyloxy] thioacetamidate	Anaerobic metabolite (no further assessed)	No data available. No assessment required.
acetonitrile	Anaerobic and photolysis metabolite (no further assessed)	No data available. No assessment required.

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 activity	Ecotoxicological activity
thiodicarb	low to high mobile (K_{oc} = 55.2 – 1006 mL / g)	LARVIN: FOCUS: no SKIPPER: FOCUS: no	Yes, but no exposure	Yes	No exposure, assessment not required
methomyl	very high mobile (K_{foc} = 13.3 – 42.8 mL / g)	LARVIN: FOCUS: no SKIPPER: FOCUS: yes	Yes	Toxicologically relevant. LD_{50} 32 mg/kg. No genotoxicity data available	Ecotoxicologically relevant (see 5.2)

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
thiodicarb (only water)	See 5.2
methomyl (water and sediment)	See 5.2

Air

Compound (name and/or code)	Toxicology
thiodicarb	High acute toxicity (LC_{50} 0.8mg/L). No data available on repeated exposure.
methomyl	No data available

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

- A shelf-life study according to Directive 94/37EC for the SC formulation (date of submission unknown identified at EPCO 20 and confirmed towards double-checking by the RMS after the expert meeting, refer to chapter 1)
- A metabolism study in cereals according to the representative use supported by the applicant to confirm the validity of the residue definition for cereals.
- A comprehensive surface water risk assessment, including drainage and runoff routes of entry in surface water, will be necessary to complete the risk assessment of the pellets formulation and the molluscicidal use (relevant for pellet formulation 'Skipper').
- The assessment of potential groundwater contamination may need to be revised, especially release rate from pellets (relevant for pellet formulation 'Skipper').
- Further data to refine acute, short-term and long-term risk to birds (relevant for pellet formulation 'Skipper'; submitted by the applicant on October 29, 2004 but not evaluated by the Rapporteur; refer to point 5.1)
- Field study on birds (Enholmes Farm, Patrington) (relevant for pellet formulation 'Skipper'; included in the dossier but not evaluated by the Rapporteur; refer to point 5.1)
- Further data to address the acute risk to birds and mammals from consumption of methomyl contaminated earthworms (relevant for pellet formulation 'Skipper'; submitted by the applicant on October 29, 2004 but not evaluated by the Rapporteur; refer to point 5.1)
- Further data to refine acute and long-term risk to mammals (relevant for pellet formulation 'Skipper'; submitted by the applicant on October 29, 2004 but not evaluated by the Rapporteur; refer to point 5.1)
- A study on acute toxicity to aquatic gastropods (relevant for both spray application ('Larvin') and pellet formulation ('Skipper'); refer to point 5.2)
- Further data to address the acute risk to earthworms from pellets on soil surface (relevant for pellet formulation 'Skipper'; refer to point 5.5)
- Further data to address the long-term risk to earthworms from exposure to methomyl (relevant for pellet formulation 'Skipper'; an interim report was submitted 29 October 2004 (not evaluated by the Rapporteur), final report expected April 2005; refer to points 5.1 and 5.5)
- Further data to clarify the risk to other non-target soil organisms (relevant for pellet formulation 'Skipper'; depends on the results for earthworms, final report expected April 2005; refer to points 5.6)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide and molluscicide as proposed by the applicant which comprises foliar spraying to control chewing and sucking insects in table and wine grapes and spreading baits to control slugs and snails in cereals.

The application rates are 0.375 kg and 0.2 kg thiodicarb per hectare, respectively. Thiodicarb can be used only as insecticide and molluscicide.
The representative formulated products for the evaluation were "Larvin" and "Skipper", a suspension concentrate (SC) and a granular bait (GB), respectively.

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 method 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.

Thiodicarb is rapidly and extensively absorbed and extensively distributed. Excretion occurs primarily as volatile components in expired air and in urine. Less than 10% is excreted in faeces. The acute toxicity is high, as well as during inhalatory exposure. Acute dermal LD_{50} is greater than 2000 mg/kg bw. It is not a skin or an eye irritant but is a skin sensitizer (Magnusson and Kligman test). Classification for acute toxicity is needed and the proposed risk phrases are: T; R23/R25 (Toxic by inhalation and if swallowed)" and R43 "May cause sensitization by skin contact".
The relevant oral NOAEL for short term exposure is 5 mg/kg bw/day. The NOAELs for chronic toxicity is 3 mg/kg bw/day. Overall, thiodicarb does not show genotoxic or carcinogenic potential. The parental and reproductive NOAELs for thiodicarb are 7 mg/kg bw/day. Due to the increased mortality of pups at dose levels which are not associated with marked maternal toxicity, classification as Cat. 2 and R61 was proposed. The NOAEL for maternal effects in the rat is 1 mg/kg bw/day; the relevant developmental NOAEL is 30 mg/kg bw/day (highest tested dose). The NOAEL for neurotoxic effects is 6 mg/kg bw/day. The **ADI is 0.01 mg/kg bw/day** with a **safety factor of 100.** The **AOEL is 0.014 mg/kg bw/day,** with a **safety factor of 500** (an additional safety factor of 5 is added)**,** due to the severity of reproductive effects. The **ARfD is 0.01 mg/kg bw,** (safety factor 100)**.** The operator exposure estimate is below the AOEL of 0.014 mg/kg bw/day for orchard sprayer activities using Larvin. For workers and bystanders the estimated exposure is below the AOEL. No data on Skipper is provided.

The metabolism of thiodicarb in fruits after foliar application is clearly understood and its main degradation product of toxicological relevance is methomyl. The residue definition proposed for both monitoring and risk assessment is the sum of thiodicarb and methomyl expressed as methomyl. No other metabolite needs to be considered in the residue definition due to its potential contribution to the toxicological burden. Ultimate degradation products of thiodicarb are acetonitrile and carbon dioxide, the last being reincorporated in endogenous plant materials.
No residues are expected to be present in following crops.
In animal the metabolism of thiodicarb is extensive and no carbamate related compound is present in edible animal commodities. There is no need for defining a residue definition for animal products or to monitor residues resulting from the representative uses of thiodicarb in these products.

In grapes and cereals, supervised residue trials support the establishment of MRLs at 1 and 0.05* mg/kg respectively. In wine the residue transfer is limited and the residue level in wine is not expected to be higher than 50 % of the residue level in raw grapes.
The risk assessment carried out for the representative uses supported by the applicant indicated an acute risk resulting from the consumption of wine and table grapes.

Under dark aerobic conditions in soil (20 - 25 °C) methomyl was the only major metabolite of thiodicarb. Unextractable residues accounted for up to 65.6 % AR and CO_2 for 30.2 % AR at the end of the studies.
Two major metabolites were identified under dark anaerobic conditions S-methyl-*N*-[*N*-methyl-*N*-(methylaminothio) carbamoyloxy] thioacetamidate and acetonitrile. Photolysis may contribute slightly to the environmental degradation of thiodicarb. Acetonitrile was the only major soil photolysis metabolite.
Thiodicarb is very low to low persistent in soil under aerobic laboratory conditions (DT_{50} = 0.13 – 1.2 d). Under the same conditions methomyl is low persistent in soils (DT_{50} = 4 – 9.9 d).
Under anaerobic conditions in laboratory degradation of thiodicarb is faster and degradation of methomyl is slightly slower than under aerobic conditions.
Whereas not triggered by the directive, field dissipation studies are available for thiodicarb formulated either as water flowable or slow release pellets.
PEC soil used in the risk assessment of LARVIN (insecticidal use) were calculated based on the worst case field half lives and either 14 d interval between applications (thiodicarb) or no degradation (methomyl). New PEC soil are now available after recalculation of half lives, but have not been used further in the assessment (see Addendum 1). RMS decided not to further assess the molluscicide use and the pellet formulation due to the number of data gaps identified at the initial assessment.
Thiodicarb is low to high mobile and methomyl is very high mobile in soil.
In sterile buffer solutions at 25 °C thiodicarb and methomyl degradation are pH dependent. Half life for thiodicarb is 0.26 d at pH 9, 30 d at pH 7 and 69 d at pH 5. The main product of thiodicarb hydrolysis is methomyl. Under the same conditions, methomyl is stable at pH 5 and pH 7 but degrades at pH 9 with a DT_{50} = 15.1 d.
Contribution of aqueous photolysis to the environmental degradation of thiodicarb and methomyl is deemed negligible. Thiodicarb is not ready biodegradable.
Thiodicarb degrades very fast to methomyl in the water phase (DT_{50} < 1 d). Levels of methomyl increase up to 17 % - 50 % AR after one day in the total system and then degraded with a half life between 21 and 29 hours.
Methomyl partitions to the sediment, reaching a maximum of 11.4 % AR in the sediment after one day in one of the systems where it was directly applied. Degradation of methomyl was also fast with half lives between 3.5 to 5 days in the total systems. Unextractable residues in the sediment reached a maximum of 21 % AR after 14 d declining to 15 % AR at the end of the study (102 d). CO_2 reached a maximum of 46 % AR at the end of the study. Acetonitrile was found in the volatiles trap to a maximum of 27 % AR. Acetonitrile was also the only metabolite that exceeds 10 % AR in the sediment phase. PEC sw of the insecticide application is calculated based on spray drift loadings.

Since thiodicarb and its metabolite methomyl are not persistent in soil it is expected that this route of entry to surface water will be dominant over run off and drainflow. However, new surface water calculations with re-evaluated worst case half lives using non linear regression (thiodicarb $DT_{50\ water}$ = 0.1 d; methomyl $DT_{50\ water}$ = 4.5 d) and a interval between applications of 28 d were presented in the addendum. In this case single application spray drift PEC sw represents the worst case that should be used for the risk assessment.

A comprehensive surface water risk assessment, including drainage and runoff routes of entry in surface water, will be necessary to complete the risk assessment of the pellets formulation and the molluscicidal use. RMS decided not to further assess the molluscicide use and the pellet formulation due to the number of data gaps identified at the initial assessment.

The potential leaching of thiodicarb and its metabolite methomyl for the insecticidal use in vines and the molluscicidal use in winter cereals was simulated with FOCUS PRZM 2.4.1 for the relevant FOCUS gw scenarios. The trigger of 0.1 µg / L was not exceeded for any of the seven scenarios simulated for the insecticidal use and was exceeded by two of the nine scenarios simulated for the molluscicidal use. The results and in particular the release rate form the pellets employed in the simulation was not discussed by the experts' meeting. As consequence, the assessment of the EU representative molluscicidal use may not be considered finalised with respect to the potential for ground water contamination.

For the insecticidal use on vines a new simulation was presented by the notifier and summarized in the addendum 1 by the RMS, using FOCUS PEARL v.2.2.2 and FOCUS PRZM v.2.4.1. Re-evaluated and normalized degradation parameters and an application interval of 28 d are used in this new modelling that confirms the results found previously.

Monitoring data on cereal cropping areas of UK show occasional breaking of the 0.1 µg / L trigger by methomyl it is not possible to know if the origin of this methomyl is from thiodicarb use or due to the application of products containing methomyl as active substance.

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

The risk assessment for terrestrial vertebrates was performed in line with the EPPO (1992) risk assessment scheme. The risk to insectivorous birds from the use of 'Larvin' as a foliar spray is considered to be low in terms of acute, short-term and long-term toxicity from the active substance, thiodicarb. With regards to the metabolite, methomyl, the assessment was refined by using the end point from the short-term dietary study converted to a daily dose. As a result, the TER value was above the Annex VI trigger and acute risk to birds from methomyl was considered to be low. The approach was discussed at the experts' meeting for ecotoxicology and it was agreed to await the opinion of the PPR panel for pirimicarb where a similar approach was used. The opinion was adopted in July 2005 and it is proposed by the EFSA that an assessment in line with the recommendations given in this opinion is conducted. The acute risk to mammals from use of 'Larvin' was considered low while the long-term risk to mammals is on the borderline of the Annex VI trigger following refinement based on residue decline in grass.

For the use of the pellet formulation ('Skipper') high acute and long-term risks were identified for birds and mammals. Additionally an acute risk from consumption of earthworms was identified.

With regard to the use of 'Larvin' risk mitigation comparable to 40 m buffer zones is required to protect aquatic organisms. With regards to 'Skipper' low risk to aquatic organisms is considered if the product is applied to undrained or peaty soils or to soils represented by Quorndon soils. If 'Skipper' is used on soils more vulnerable to drainage, there is a high potential risk for exposure of surface water via drainage and risk mitigation measures must be considered at Member state level. Additionally contamination of surface water from run-off should be considered. Before the risk assessment for the aquatic environment can be finalised a study on acute toxicity to aquatic gastropods should be conducted and evaluated.

Thiodicarb is toxic to honeybees. However, field data are available showing that after 12 hours residues were non-toxic. For 'Larvin' risk mitigation measures, e.g. applications outside flowering or in the evening are proposed to be considered at Member State level. The risk to bees from use of 'Skipper' is considered low. For non-target arthropods there is a potential for recolonization since residue decline is relatively rapid, effects on mortality and reproduction are below 50% in 5-7 days aged residue studies, and in the case of 'Larvin' less than 50% mortality is expected for the most sensitive species tested at 3 m distance from the treated field. However, the EPCO experts' meeting for ecotoxicology was of the opinion that oral route of exposure had not been sufficiently addressed in the studies and risk mitigation measures for the use of 'Larvin' should therefore be considered at Member State level.

For the use of 'Skipper' the acute risk to earthworms from pellets on the soil surface needs to be addressed. Additionally, a long-term risk to earthworms from the exposure to methomyl was identified. A field study to address the risk is ongoing. Pending the evaluation of new data, the risk assessment for earthworms for the use of 'Skipper' cannot be finalised. The risk to soil microbial processes and to non-target flora is low.

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

- Risk mitigation measures comparable to 40 m buffer zones are needed to protect aquatic invertebrates (foliar application ('Larvin'), refer to point 5.2).
- Risk mitigation measures should be considered at Member State level for soils with a potential for leakage via drainage (pellet formulation ('Skipper'), refer to point 5.2).
- Risk mitigation measures for foliar application, such as spraying outside flowering of weeds or in the evening, should be considered at Member State level to reduce the risk to bees ('Larvin', refer to point 5.3).
- Risk mitigation measures for foliar application, such as buffer zones, should be considered at Member State level to reduce the risk to non-target arthropods ('Larvin', refer to point 5.4).

Critical areas of concern

- Thiodicarb is highly toxic during acute oral and inhalatory exposure.
- There is an acute dietary risk identified for toddlers resulting from the consumption of treated table grapes and for adults resulting from the consumption of wine.

Larvin

- A high acute risk to birds was identified in the first tier assessment. It is proposed that the assessment is refined by using the short-term dietary endpoint in line with the recommendations given in the PPR panel opinion for pirimicarb.
- The long-term risk to herbivorous mammals is slightly below or just at the Annex VI trigger value when the risk assessment is conducted according to the EPPO scheme. A new risk assessment in line with SANCO/4145/2000 is proposed by the EFSA.
- A high risk was identified for the aquatic environment. Risk mitigation measures such as 40 m buffer zones are needed to protect aquatic invertebrates.
- A high risk to honeybees was identified. Risk mitigation measures for foliar application, such as spraying outside flowering of weeds and in the evening, should be considered at Member State level.
- The risk to non-target arthropods from oral exposure following spray application was not considered fully addressed by the experts' meeting. Risk mitigation measures should be considered at Member State level.

Skipper

- No operator exposure estimates with this formulation are provided.
- MS should pay attention to potential ground water contamination under vulnerable situations.
- A high acute, short-term and long-term risk to birds from direct consumption of pellets was identified.
- A high acute risk was identified for birds consuming methomyl contaminated earthworms.
- High acute and long-term risks to mammals from direct consumption of pellets were identified.
- A high acute risk was identified for mammals consuming methomyl contaminated earthworms for the use of 'Skipper'.
- A high risk was identified for the aquatic environment from the use on soils with a potential for leakage via drainage. Risk mitigation measures should be considered at Member State level.
- A high long-term risk to earthworms was identified. Pending the results from an ongoing field study, no final conclusion on the risk to earthworms can be drawn.

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

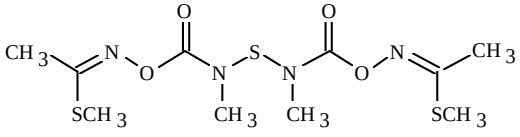
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	Thiodicarb
Function (e.g. fungicide)	Molluscicide, insecticide

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

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	3,7,9,13-tetramethyl-5,11-dioxa-2,8,14-trithia-4,7,9,12-tetra-azapentadeca-3,12-diene-6,10-dione
Chemical name (CA) ‡	dimethyl N,N'- [thiobis [(methylimino) carbonyloxy]] – bis (ethanimidothioate)
CIPAC No ‡	543
CAS No ‡	59669-26-0
EEC No (EINECS or ELINCS) ‡	261-848-7
FAO Specification ‡ (including year of publication)	AGP:CP/351 Published in 1997 The thiodicarb content shall be declared (not less than 940 g/kg) and, when determined, the content obtained shall not differ from that declared by more than ± 20 g/kg 5 g/kg methomyl
Minimum purity of the active substance as manufactured ‡ (g/kg)	940g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	5 g/kg methomyl
Molecular formula ‡	$C_{10}H_{18}N_4O_4S_3$
Molecular mass ‡	354.5
Structural formula ‡	 Thiodicarb

‡ 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) ‡	172.6 ºC purity 99.9%
Boiling point (state purity) ‡	No boiling point observed
Temperature of decomposition	184.7 ºC purity 99.9%
Appearance (state purity) ‡	White powder purity 99..9% Off-white powder purity 94.1%
Relative density (state purity) ‡	1.47 g/ml at 20 ºC purity 99.9% 1.48 g/ml at 20 ºC purity 94.1% Density reported not relative density
Surface tension	71.97 $mN.m^{-1}$ purity 94.1%. The test concentration was circa 20 mg/L.
Vapour pressure (in Pa, state temperature) ‡	2.7 x 10-3 @ 25 ºC purity 99.9%
Henry's law constant (Pa m^3 mol^{-1}) ‡	$4.31x10^{-2}$ Pa m^3 mol^{-1} @ 25 ºC
Solubility in water ‡ (g/L or mg/L, state temperature)	22.19 mg/L deionised water at 25 ºC purity 99.9% 24.47 mg/L pH 7 at 25 ºC 26.88 mg/L pH 3 at 25 ºC 29.83 mg/L pH 5 at 25 ºC
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	Ethanol 0.97 g/L n-hexane 0.32 g/L Toluene 0.92 g/L Dichloromethane 200-300 g/L Acetone 5.33 g/L Ethylacetate 1.79 g/L All carried out at 20 ºC purity 99.9%
Partition co-efficient (log POW) ‡ (state pH and temperature)	1.62 in unbuffered water purity 99.9 %
Hydrolytic stability (DT_{50}) ‡ (state pH and temperature)	69 days at pH 5 31 days at pH 7 0.26 days at pH 9 All tests were carried at 25 ºC purity > 99%.
Dissociation constant ‡	Thiodicarb does not dissociate
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	232-234 nm ε ~ 18000 $L.mol^{-1}.cm^{-1}$ purity 99.9% ε < 10 at ≥ 290 nm
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	7.6 days at pH 6
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	ε < 10 $l.mol^{-1}.cm^{-1}$
Flammability ‡	Not flammable
Explosive properties ‡	Not 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 (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Table and wine grapes	Northern + Southern Europe	Larvin, Securex Souverain	F	Chewing and sucking insects	SC	375 g/L	Foliar spray	Before flowering BBCH 55	2	28 d 2 nd treat-ment at max. BBCH 85	0.0375	1000	0.375	35	**[1]**
Wheat, Triticale, Rye, Barley, Oats	Northern + Southern Europe	Skipper Genesis	F	Slugs and snails	GB	40 g/kg	Admixtu re with seed	At drilling	1	-			0.2#		**[2]**
Wheat, Triticale, Rye, Barley, Oats	Northern + Southern Europe	Skipper Genesis	F	Slugs and snails	GB	40 g/kg	Broadca st	Up to begin of stem elongation BBCH 30	1 - 3	Not specified			0.2#		**[2]**

[1] The risk assessment revealed a risk in section 3.
[2] The risk assessment could not be concluded as the Rapporteur has not evaluated the recently submitted information on Skipper (primarily on Ecotox).
For Skipper/Genesis the maximum total dose when applied in admixture with cereal seed and broadcast application is 0.6 kg as/ha.

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)	The technical material is analysed by the appropriate CIPAC method.
Impurities in technical as (principle of method)	Gravimetric, ICP-MS and HPL-UV
Plant protection product (principle of method)	HPLC-UV at 254 nm

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	LC-MS/MS LOQ=0.01 mg/kg analytes thiodicarb and methomyl Except cottonseed 0.02 mg/kg, wheat forage and wheat straw 0.04 mg/kg
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not applicable as significant residues are not expected in animal feed items.
Soil (principle of method and LOQ)	HPLC-fluorescence LOQ=0.001 mg/kg analytes thiodicarb and methomyl
Water (principle of method and LOQ)	HPLC-fluorescence LOQ=0.1 µg/L analytes thiodicarb and methomyl Surface water and drinking water
Air (principle of method and LOQ)	HPLC-UV at 234 nm LOQ 3 µg/ m^3 analytes thiodicarb and methomyl
Body fluids and tissues (principle of method and LOQ)	Human urine HPLC with a fluorescence LOQ = 10 µg/L analytes thiodicarb and methomyl

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	No classification required.

‡ 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 (C_{max} *ca* 1 hour at 2 mg/kg bw) and extensive (>70 - 90%)
Distribution ‡	Extensive; highest concentration in erythrocytes
Potential for accumulation ‡	Low, with the exception of erythrocytes
Rate and extent of excretion ‡	Rapid (mainly in 0 – 12 hour samples) and extensive; significant proportion as exhaled volatiles (40%)
Metabolism in animals ‡	Very extensive, primary excretion as acetonitrile and CO_2; retained radiolabel may be in the form of simple carbon compounds incorporated into biomolecules
Toxicologically significant compounds ‡ (animals, plants and environment)	Thiodicarb and methomyl

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	50 mg/kg bw **R23**
Rat LD_{50} dermal ‡	>2000 mg/kg bw
Rat LC_{50} inhalation ‡	0.66 mg/L **R25**
Skin irritation ‡	Not irritant
Eye irritation ‡	Mild, transient irritant (no classification proposed)
Skin sensitization ‡ (test method used and result)	Positive (M&K); negative in human patch test **R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Cholinesterase inhibition, clinical signs (including tremors) red cell effects (mild macrocytic anaemia) & associated splenic findings,
Lowest relevant oral NOAEL / NOEL ‡	5 mg/kg bw/d (6-month and 1-year dog studies)
Lowest relevant dermal NOAEL / NOEL ‡	No NOAEL possible to be determined due to poor quality of the studies
Lowest relevant inhalation NOAEL / NOEL ‡	LOAEL 0.005 mg/L, lowest dose tested

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

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	Some positive results in vitro, negative in vivo. Overall, no genotoxic potential

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

Target/critical effect ‡	Macrocytic anaemia, splenic effects (haemosiderin deposition, extramedullary haematopoiesis); liver hyperplasia in mice
Lowest relevant NOAEL / NOEL ‡	3 mg/kg bw/d
Carcinogenicity ‡	Liver tumours in mice at toxic doses. Clear NOAEL identified (12 mg/kg bw/day). Unlikely to pose a risk to humans

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Reduced pup viability and weight
Lowest relevant reproductive NOAEL / NOEL ‡	Maternal and reproductive: 7 mg/kg bw/d
Developmental target / critical effect ‡	Not teratogenic; no specific embryo- / foetotoxicity (rats & rabbits)
Lowest relevant developmental NOAEL / NOEL ‡	Maternal: 1 mg/kg bw/day Developmental: >30 mg/kg bw/d (rats)

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

Acute (gavage)	<5 mg/kg bw ; cholinesterase inhibition; no neuropathy
90 day (diet)	6 mg/kg bw/d; no neuropathy

Other toxicological studies ‡ (Annex IIA, point 5.8)

Metabolites	Methomyl: ADI and ARfD 0.0025 mg/kg bw/day*

* Values currently agreed for the assessment of methomyl

Medical data ‡ (Annex IIA, point 5.9)

.....	Nothing adverse in production workers

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

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw/day	Rat development, maternal toxicity; supported by rat acute neurotoxicity study	100
AOEL (systemic) ‡	0.014 mg/kg bw/day	Rat reproduction (diet) pup survival and body weight	500
ARfD ‡ (acute reference dose)	0.01mg /kg bw/day	Rat development, maternal toxicity; supported by rat acute neurotoxicity study	100

Dermal absorption (Annex IIIA, point 7.3)

	Value	Basis
Larvin	0.15% (concentrate) 1.0% (dilutions 1:≤220) 3% (dilutions 1:>220)	Based on *in vitro* data with rat and human skin samples
Skipper (granule)	No data	

Acceptable exposure scenarios (including method of calculation)

Larvin

Operator	Estimates of exposure for an operator applying 'Larvin' as a foliar spray, indicate that the exposure estimate is below the AOEL for orchard spraying activities only when PPE is used (German model, 21%); for hand-held activities, exposure does not exceeds the AOEL even without PPE (German model, 71%) or with PPE (UK POEM, 73%)
Workers	Estimates of exposure, based on the German re-entry model, indicate an exposure to Larvin below the AOEL (16%)
Bystanders	Levels of systemic exposure to bystanders, based on German and UK data, are below the AOEL (5%)

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

Skipper

Operator	No data available
Workers	No data available
Bystanders	No data available

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	T;	Toxic;
	R23/25,	Toxic by inhalation and if swallowed;
	R43,	Toxic by inhalation and if swallowed; May cause sensitisation by skin contact:
	Cat 2 R61	May cause harm to unborn child

‡ 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
Rotational crops	Mustard Greens, Cabbage and Wheat. Plant back intervals were 31, 125 and 364 days.
Plant residue definition for monitoring	Sum of thiodicarb and methomyl expressed as methomyl
Plant residue definition for risk assessment	Sum of thiodicarb and methomyl expressed as methomyl
Conversion factor (monitoring to risk assessment)	1

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

Animals covered	Hens, Goat, Cow
Animal residue definition for monitoring	Not proposed as no animal intakes above 0.1 mg/kg diet
Animal residue definition for risk assessment	Not proposed as no animal intakes above 0.1 mg/kg diet
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Not applicable
Fat soluble residue: (yes/no)	Not applicable

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

.....	No residue expected under normal application according to the representative use.

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

.....	Tomatoes stable for 9 months Apples stable for 14 months Grain stable for at least 12 months Grape in line with apples Sorghum stable for 6 months

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

Not applicable

‡ 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)
Barley grain Barley straw	S	<0.04x5 <0.04 x 4, 0.052	Data support the molluscide use.	0.05*	0.04
Wheat grain Wheat straw	S	<0.04 x 5 <0.04 x 5	Data support the molluscide use.	0.05*	0.04
Barley grain Barley straw	N	<0.04 x 3 and <0.05 0.04 x 3 and <0.2	Data support the molluscide use.	0.05*	0.04
Wheat grain Wheat straw	N	<0.04 x 5 and <0.05 <0.2	Data support the molluscide use.	0.05*	0.04
Grapes	S	0.047, 0.07, 0.12, 0.22, 0.23, 0.25, 0.34, 0.52, 0.66		1	0.23
Grapes	N	0.11, 0.12, 0.13, 0.14, 0.20, 0.26, 0.46, 0.60, 0.72		1	0.20

(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 bw/day (methomyl)
IEDI (European Diet) (% ADI)	WHO 84 % of the ADI for cereals, grapes and wine intakes.
NEDI (% ADI)	UK Highest total from cereals and grapes was 60 % of the ADI (toddlers)
Factors included in NEDI	Reduction of 0.5 from grapes to wine and the STMR
ARfD	0.0025 mg/kg bw (methomyl)
Acute exposure (% ARfD)	Wheat: adult 8 %, toddler 16 % Table grapes: adult 392 %, toddler 1560 % Wine grapes: adult 136 %, toddler not applicable

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Grapes to wine	4	0.5	-

* 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)

Cereals	0.05* mg/kg
Wine and table grapes	1 mg/kg

*) Indicates that the MRL is set at the limit of quantification of the method of analysis

‡ 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 ‡	At 20ºC, after 56 days (study end), 59.37-65.56%AR (3 soils). [Acetyl-1-14^C] thiodicarb label.
Non-extractable residues after 100 days ‡	At 20ºC, after 56 days (study end) 26.06-30.22%AR (3 soils). [Acetyl-1-14^C] thiodicarb label.
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	Methomyl: up to 79.76% (day 1); 0.28-2.48% AR (day 56 (study end)) at 20ºC.

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

Anaerobic degradation ‡	Volatiles – 1.83% after 4 hours (study end). Non-extractable residues – 5.29 % after 4 hours (study end). Acetonitrile: up to 77.9% AR (74 minutes); 75.2% at 4 hours (study end). S-Methyl-*N*-[*N*-methyl-*N*-(methylaminothio) carbomoyloxy] thioacetimidate: up to 28.2% (8 minutes); 0.9% at 4 hours. [Acetyl-1-14^C] thiodicarb label (study end).
Soil photolysis ‡	Volatiles - 44.11% after 21 days (study end). Non-extractable residues 29.75% after 21 days (study end). DT_{50} = 0.8 days for irradiated, 0.33 days for dark controls in 21 day study. 26.91% AR remaining on dark controls after 21 days, compared with 24.88% on irradiated plates. 10.78hr light/13.22hr dark cycle, average 384Wm^{-2} at soil surface. Methomyl found at up to 92.32% AR (at 2 days). DT_{50} of methomyl in dark control = 9.70 d [Acetyl-1-14^C] thiodicarb label.

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

Method of calculation	Degradation in lab and dissipation in field studies followed simple first order kinetics.

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

Laboratory studies ‡ (range or median, with n value, with r^2 value)	Thiodicarb DT_{50lab} (20°C, aerobic): 0.13-1.2 days, (4 soils, r^2 = 0.97-1.00). Geometric Mean 1st order 20ºC, –10kPa value for FOCUS models 0.39 days. Methomyl DT_{50lab} (20°C, aerobic): 4-9.9 days, (7 soils, r^2 = 0.97-1.00). DT_{50lab} (25°C, aerobic): 10.5 days (1 soil, r^2 = 0.99). Median 1st order 20ºC, –10kPa value for FOCUS models 5.81 days. Thiodicarb DT_{90lab} (20°C, aerobic): 0.42-3.9 days, (4 soils, r^2 = 0.97-1.00). Methomyl DT_{90lab} (20°C, aerobic): 14.0-33.0 days, (7 soils, r^2 = 0.97-1.00). DT_{90lab} (25°C, aerobic): 35 days, (1 soil, r^2 = 0.99). Thiodicarb DT_{50lab} (10°C, aerobic): 1.7 days (1 soil, r^2 = 0.96). DT_{90lab} (10°C, aerobic): 5.7 days (1 soil, r^2 = 0.96). Methomyl DT_{50lab} (10°C, aerobic): 23.2 days (1 soil, r^2 = 0.96). DT_{90lab} (10°C, aerobic): 77.0 days (1 soil, r^2 = 0.96). Thiodicarb DT_{50lab} (20°C, anaerobic): (total system) 6 minutes (1 soil, r^2 = 0.98). Methomyl DT_{50lab} (25°C and 20°C, anaerobic): (total system) 235 minutes - 14 days (2 soils, r^2 = 0.91 and 0.98).
	Degradation in the saturated zone: no data submitted and no data required.

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

Field studies ‡ (state location, range or median with n value)	DT_{50f}: 1) 1 site (N USA at 6.7 kg a.s./ha), 6x1.2kg applications, parent and methomyl analysed. DT_{50}field thiodicarb (simple 1st order) = 18 days, r^2 = 0.89. DT_{50}field methomyl (simple 1st order) = 43.1 days (Nov-Mar), 17.6 days (Mar-May), r^2 = 1.00. Realistic worst case DT_{50} of 18 days (simple 1st order) used for PECsoil. 2) 1 site (S USA at 3.36 kg a.s./ha), 1 x 3.36 kg application, parent and methomyl analysed. DT_{50}field thiodicarb (simple 1st order) = 4 hours. DT_{50}field methomyl (simple 1st order, surface) = 2 days; DT_{50}field methomyl (simple 1st order, subsurface) = 0.5 – 1.6 months. Lab data used for $FOCUS_{GW}$ modelling. DT_{90f}: Thiodicarb (simple 1st order) = 58.6 days, r^2 = 0.89. Methomyl (simple 1st order) = 143.7 days (Nov-Mar), 58.7 days (Mar-May), r^2 = 1.00.
Soil accumulation and plateau concentration ‡	No data supplied, none required.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	Thiodicarb K_{oc} = 55.2-1005.7 ml/g (mean 417.7 ml/g), 4 soils, pH 6.5-7.4, %om 0.5-2.4. Freundlich coeff. (1/n) = 1.20-1.35 (mean 1.29). No pH relationship observed. Methomyl K_{foc} = 13.3-42.8 ml/g (mean 25.2 ml/g), 5 soils, pH 5.1-8.1, %om 1.71-3.91. Freundlich coeff. (1/n) = 0.82-0.89 (mean 0.86). No pH relationship observed. Mean K_{oc}/Kf_{oc} and 1/n values used for $FOCUS_{GW}$ modelling.

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

Column leaching ‡	No data submitted, none required.
Aged residues leaching ‡	Study submitted of limited value (ageing period 5xDT_{50} – see B.8.2.2a).
Lysimeter/ field leaching studies ‡	No data submitted, none required.

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

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	1) Insecticidal use on vines: 70% interception, soil density 1.5 g/ml, top 5 cm soil layer, 1st order DT_{50} field = 18d. Methomyl: formation = 79.8%; no degradation between applications. 2) Molluscicidal use on cereals: Not fully assessed
Application rate	Insecticidal use on vines: 2 x 375 g a.s./ha with 14 day spray interval. Molluscicidal use on cereals: Not fully assessed

$PEC_{(s)}$ mg/kg	Parent (Methomyl) 2x375g/ha Actual	Parent (Methomyl) 3x200g/ha Actual
Initial/Maximum	0.237 (0.218)	Not fully assessed

Note: PEC soil based on DT_{50} lab = 1.2 d and 28 d interval between applications are provided in Addendum 1. Not used in the EU risk assessment.

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) ‡ (state pH and temperature)	pH 5: Thiodicarb: At 25ºC, DT_{50} = 69.1 days. Methomyl: At 25ºC, stable to hydrolysis. pH 7: Thiodicarb: At 25ºC, DT_{50} = 30.8 days. Methomyl: At 25ºC, stable to hydrolysis. pH 9: Thiodicarb: At 25ºC, DT_{50} = 0.26 days. Methomyl: At 25ºC, DT_{50} = 15.1 days.
Photolytic degradation of active substance and relevant metabolites ‡	Natural sunlight study carried out at pH6 and 25ºC in North Carolina, USA (35º55'N 78º50'W) September 9 – October 2. DT_{50} 9 days. Methomyl only major degradation product (24% AR at 23 days).
Readily biodegradable (yes/no)	No (OECD 301b study).

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

Degradation in water/sediment	- DT_{50} water - DT_{90} water - DT_{50} whole system - DT_{90} whole system	Thiodicarb Aerobic lab sediment/water at 20°C (to BBA guidelines), in two systems (natural water and sediment). Total system DT_{50} < 1 hour both systems. Distribution between water and sediment phases not reported except for unextractables. Methomyl only major (> 10% AR) metabolite identified, at 50.0% and 17.4% (both at 24 hours). Methomyl DT_{50} 21-29 hours.
Mineralisation		Methomyl Three aerobic lab sediment/water studies at 20°C (study (i) to SETAC guidelines, study (ii) to BBA and NOHSAN). (iii) to BBA – study conducted with thiodicarb as parent material. All studies used two systems of natural water and sediment.
Non-extractable residues in sediment		i) Total system DT_{50} 0.93 – 6.2 days. Water phase dissipation DT_{50} 2.5 – 4.5d (non-linear 1st order). No major metabolites.
Distribution in water / sediment systems (active substance)		ii) Total system DT s of 3.5 and 4.8 days, water DT_{50}s 3.5 and 3.9 days. Acetonitrile only major metabolite (sediment).
Distribution in water / sediment systems (metabolites)		iii) Water phase dissipationDT_{50} 1.3 – 1.5d (non-linear 1st order).
		Thiodicarb CO_2 70.6% and 75.0% (100 days). Unextractables: 0.1% and 0.1% (100 days, water); 14.1% and 14.8% (100 days, sediment).
		Methomyl i) CO_2: 60.8% - 73.6% at study termination. Unextractables: 15.25% - 15.49% at study termination (total system). ii) CO_2: 32.1% - 46.2% at study termination. Unextractables: 10.0% - 14.7% at study termination (sediment).

‡ 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	Vines Thiodicarb: Overall 90th %ile (1 application), 82nd %ile (2 applications) spray drift values at 3, 5, 10, 15, 20, 30 and 40 m, water 1st order DT_{50} = 0.1 day, 1 crop, 30cm deep water body. Thiodicarb will degrade between applications. Metabolites: The major metabolite methomyl (DT_{50} = 4.5 days) is considered to be the main driver of the risk assessment. 100% transformation assumed. Values calculated at 3, 5, 10, 15, 20, 30 and 40m. Winter cereals Not fully assessed
Application rate	Vines: 2 x 375 g a.s./ha, 28 day application interval. Winter cereals: up to 3 x 200 g a.s./ha, 14 day application interval.
Main routes of entry	Vines: Spray drift Winter cereals: Not fully assessed.

Instantaneous PECsurface water for thiodicarb residue (µg/kg) from spray drift (late use on vines)

Distance from water body (m)	Single application (worst case used in EU assessment)		Two applications	
	90th percentile drift rate	Initial PECsw (µg/L)	82nd percentile drift rate	Initial PECsw (µg/L)
3	8.02	10.03	7.23	9.04
5	3.62	4.53	3.22	4.03
10	1.23	1.54	1.07	1.34
15	0.65	0.81	0.56	0.70
20	0.42	0.53	0.36	0.45
30	0.22	0.28	0.19	0.24
40	0.14	0.18	0.12	0.15

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

Instantaneous PEC surface water for methomyl residue (µg/kg) from spray drift (late use on vines)

Distance from water body (m)	Single application (worst case used in EU assessment)		Two applications	
	90th percentile drift rate	Initial PECsw (µg/L)	82nd percentile drift rate	Initial PECsw (µg/L)*
3	8.02	9.18	7.23	8.38
5	3.62	4.14	3.22	3.73
10	1.23	1.41	1.07	1.24
15	0.65	0.74	0.56	0.65
20	0.42	0.48	0.36	0.42
30	0.22	0.25	0.19	0.22
40	0.14	0.16	0.12	0.14

*Peak concentration occurred immediately following the second application

PEC (sediment)

Parent

Method of calculation	From the water/sediment studies supplied, concentrations of parent thiodicarb and the metabolite methomyl are expected to be negligible. PEC sediment of parent not calculated
Application rate	N/A.

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	FOCUS gw modelling – used model FOCUS-PRZM 2.4.1. DT_{50} from geometric mean lab study, normalised to 20ºC and -10kPa. Thiodicarb: DT_{50}: 0.39 days (vines and cereals): 50% pellet release time 2.1 days (winter cereals only). Mean Kfoc 417.7 ml/g, mean Freundlich coeff. (1/n) 1.29. Methomyl: DT_{50}: 5.81 days, mean Kfoc 25.2 ml/g, mean Freundlich coeff. (1/n) 0.86. 93.7% formation from thiodicarb.

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

	i) Molluscicidal use - 9 scenarios, according to FOCUS gw guidance. Crop: winter cereals. ii) Insecticidal use – 7 scenarios, according to FOCUS gw guidance. Crop: vines.
Application rate	i) Winter cereals: 3x200 g a.s./ha (3x200 g a.s./ha with 0% crop interception), 1st application at emergence, following applications at 14 day intervals. Vines: 2x375 g a.s./ha (2x112.5 g a.s./ha with 70% crop interception), applied 31st May and 28th June.

$PEC_{(gw)}$

Maximum concentration	Not reported, not required.
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Thiodicarb: <0.001 µg/L all scenarios for both uses. Methomyl: i) Winter cereals: Not fully assessed. Preliminary, results show potential for contamination of ground water at levels above 0.1 µg/L under vulnerable situations. Release rate from pellets not fully agreed during the Peer Review. ii) Vines: <0.001 µg/L all scenarios.

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

Direct photolysis in air ‡	Not applicable.
Quantum yield of direct phototransformation	Not calculated
Photochemical oxidative degradation in air ‡	DT_{50} of 9.7 hours (Atkinson calculation)
Volatilization ‡	From soil: 90% recovery AR (21 days)
	Vapour pressure: 2.7 x 10^{-3} kPa @ 25ºC Henrys Law constant: 4.31 x 10^{-2} $Pa.m^3.mol^{-1}$ @ 25ºC

PEC (air)

Method of calculation	Assessment by RMS.

$PEC_{(a)}$

Maximum concentration	Negligible

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

Definition of the Residue (Annex IIA, point 7.3)

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

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

Soil (indicate location and type of study)	Adequate monitoring data not available.
Surface water (indicate location and type of study)	For the UK, data from 1992 to 2003 have been evaluated with no samples analysed for thiodicarb. However during this period methomyl was monitored for in surface in the UK and these are summarised below. A total of 2028 surface water samples were collected and analysed from the Anglian region of the UK.

Year	1st October – 30th March		1st April – 30th September	
	No. of samples	Max. conc (µg/L)	No. of samples	Max. conc (µg/L)
1992	95	<LOQ	102	<LOQ
1993	94	<LOQ	153	<LOQ
1994	128	0.05	125	0.11
1995	119	0.43	89	<LOQ
1996	211	0.19	212	0.72
1997	101	0.16	119	1.63
1998	99	0.16	94	0.25
1999	No data	No data	No data	No data
2000	No data	No data	No data	No data

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

Year	1st October – 30th March		1st April – 30th September	
	No. of samples	Max. conc (µg/L)	No. of samples	Max. conc (µg/L)
2001	53	<LOQ	69	<LOQ
2002	40	<LOQ	31	<LOQ
2003	41	0.14	53	<LOQ
Total	981		1047	

LOQ = 0.025µg/L

Ground water (indicate location and type of study)	For the UK, data from 1992 to 2003 have been evaluated with no samples analysed for thiodicarb. However during this period methomyl was monitored for in groundwaters in the UK and these are summarised below. A total of 504 groundwater samples were collected and analysed from the Anglian region of the UK.

Year	1st October – 30th March		1st April – 30th September	
	No. of samples	Max. conc (µg/L)	No. of samples	Max. conc (µg/L)
1992	40	<LOQ	38	<LOQ
1993	1	<LOQ	28	<LOQ
1994	3	<LOQ	3	<LOQ
1995	7	<LOQ	1	<LOQ
1996	0	<LOQ	11	0.42
1997	16	0.03	21	0.03
1998	38	0.15	38	<LOQ
1999	No data	No data	No data	No data
2000	No data	No data	No data	No data
2001	48	<LOQ	76	<LOQ
2002	36	<LOQ	52	<LOQ
2003	21	<LOQ	26	<LOQ
Total	210		294	

LOQ = 0.025µg/L

Air (indicate location and type of study)	Adequate monitoring data not available.

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Not readily biodegradable. Candidate for R53.

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

Appendix 1.6: Effects on non-target Species

Larvin

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

Acute toxicity to mammals ‡	LD_{50} = 50 mg thiodicarb/kg bw/d (rat) Acute NOEL (mortality) = 202 mg thiodicarb/kg bw/d (mouse)
Acute toxicity to birds ‡	LD_{50} = 2023 mg thiodicarb/kg bw/d (bobwhite quail) LD_{50} = 24.2 mg methomyl/kg bw/d (bobwhite quail)
Dietary toxicity to birds ‡	LC_{50} > 5620 ppm thiodicarb (bobwhite quail and mallard duck) LC_{50} = 3952 ppm methomyl (658 mg/kg bw/day) (mallard duck)
Reproductive toxicity to birds ‡	NOEC = 500 ppm thiodicarb (mallard duck) NOEC (parental) = 150 ppm methomyl (mallard duck) NOEC (reproductive) = 500 ppm methomyl (mallard duck)
Reproductive toxicity to mammals ‡	NOAEL = 100 ppm thiodicarb (rat) NOAEL = 84 ppm thiodicarb (rat)

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
Thiodicarb					
0.375 x 2	Grapevines	Insectivorous bird	Acute	258	10
0.375 x 2	Grapevines	Insectivorous bird	Short-term	> 517	10
0.375 x 2	Grapevines	Insectivorous bird	Long-term	64	5
0.375 x 2	Grapevines	Small herbivorous mammal	Acute	15.3	10
0.375 x 2	Grapevines	Small herbivorous mammal	Long-term	4.95[1]	5
0.375 x 2	Grapevines	Insectivorous mammal	Acute	68.6	10
0.375 x 2	Grapevines	Insectivorous mammal	Long-term	98.7	5

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
Methomyl					
0.375 x 2	Grapevines	Insectivorous bird	Acute	3.4	10
0.375 x 2	Grapevines	Insectivorous bird	Acute (refined)	92.3	10
0.375 x 2	Grapevines	Insectivorous bird	Short-term	399.2	10
0.375 x 2	Grapevines	Insectivorous bird	Long-term (reproductive)	50.5	5
0.375 x 2	Grapevines	Insectivorous bird	Long-term (parental)	15	5

[1]Calculated using the lowest NOAEL for rats

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 test substance/L)
Laboratory tests				
Lepomis macrochirus	thiodicarb	96 h	Mortality LC_{50}	1.4
Pimephales promelas	thiodicarb	35 d	Growth NOEC	0.025
Daphnia magna	thiodicarb	48 h	Mortality EC_{50}	0.027
Chironomus riparius	thiodicarb	28 d	Reproductive NOEC	0.080
Pseudokirchneriella subcapitata	thiodicarb	96 h	Biomass EC_{50}	18
Lepomis macrochirus	methomyl	96 h	Mortality LC_{50}	0.62
Daphnia magna	methomyl	48 h	Mortality EC_{50}	0.017
Daphnia magna	methomyl	21 d	Reproductive NOEC	0.0016
Pseudokirchneriella subcapitata	methomyl	72 h	Biomass EC_{50}	94
Oncorhynchus mykiss	'Larvin'	96 h	Mortality EC_{50}	8.83
Daphnia magna	'Larvin'	48 h	Mortality EC_{50}	0.29

Microcosm or mesocosm tests
Not required.

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

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
Thiodicarb						
0.375	Grapevines (late)	*Lepomis macrochirus*	96 h	3	140	100
0.375	Grapevines (late)	*Daphnia magna*	48 h	30	98	100
0.375	Grapevines (late)	*Pseudokirchneriella subcapitata*	96 h	3	1800	10
Methomyl						
0.375	Grapevines (late)	*Lepomis macrochirus*	96 h	40	3949	100
0.375	Grapevines (late)	*Daphnia magna*	48 h	40	108.3	100
0.375	Grapevines (late)	*Pseudokirchneriella subcapitata*	72 h	3	9936.6	10
0.375	Grapevines (late)	*Pimephales promelas*	35 d	40	159.2	10
0.375	Grapevines (late)	*Daphnia magna*	21 d	40	10.2	10
0.375	Grapevines (late)	*Chironomous riparius*	28 d	40	509.6	10
'Larvin'						
0.375	Grapevines (late)	*Oncorhynchus mykiss*	96 h	3	330.7	100
0.375	Grapevines (late)	*Daphnia magna*	48 h	30	395	100

Bioconcentration

Bioconcentration factor (BCF) ‡	6.3
Annex VI Trigger:for the bioconcentration factor	100 for compound not readily biodegradable
Clearance time (CT_{50}) (CT_{90})	12 +/- 0.81 days Not determined
Level of residues (%) in organisms after the 14 day depuration phase	52%

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

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

Acute oral toxicity ‡	48 h LD_{50} = 0.153 µg a.s./bee based on active substance 72 h LD_{50} = 0.184 µg a.s./bee based on 'Larvin''
Acute contact toxicity ‡	48 h LD_{50} = 3.1 µg a.s./bee based on active substance 72 h LD_{50} = 1.56 µg a.s./bee based on 'Larvin'

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
Thiodicarb				
0.375	Grapevines	Oral	2451	50
0.375	Grapevines	Contact	121	50
'Larvin'				
0.375	Grapevines	Oral	2038	50
0.375	Grapevines	Contact	240	50

Field or semi-field tests
'Larvin 3.2' (equivalent to 'Larvin') at 560 g a.s./ha suppressed bee visits by 16% over 3 days and killed on average 206 bees over a 3 day period. The residues were non-toxic to bees after 12 hours.

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

Species	Stage	Test Substance	Dose (g as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests – Glass plate						
Aphidius rhopalosiphi	Adult	Larvin	0.4, 0.21, 0.42, 0.84, 1.7	Mortality	LR_{50} = 0.4 g a.s./ha	30%
Typhlodromus pyri	Protonymph	Larvin	21, 42, 84, 169, 337	Mortality	LR_{50}>337 g a.s./ha This end point is not reliable as there was a poor dose response.	30%

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

Species	Stage	Test Substance	Dose (g as/ha)	Endpoint	Effect	Annex VI Trigger
Orius laevigatus	2nd nymph	Larvin	21, 42, 84, 169, 337	Mortality	LR_{50} = 25.4 g a.s./ha	30%
Chrysoperla carnae	Larvae	Larvin	18.75, 375	Mortality	No effects	30%
Trichogramma cacoeciae	Adult	Larvin	75	Reduction in parasitic capacity	100%	30%
Aphidius rhopalosiphi	Adult	Methomyl 20 SL	0.006, 0.019, 0.056, 0.167, 0.5	Mortality	LR_{50} = 0.25 g a.s./ha	30%
Laboratory tests – extended. The trigger value in Directive 97/57/EC is 30% (ESCORT2 refers to values of 50% for extended laboratory studies)						
Aphidius rhopalosiphi	Adult	Larvin aged on barley	4.0 25.6 375 638	Mortality Reproduction Mortality Reproduction Mortality Reproduction Mortality Reproduction	Fresh residues 0% 30.1% (Control = 27.4%) 0% 21.0% (Control = 27.4%) 6-d old residues 0% 22% (Control = 18.5%) 0% 26.9% (Control = 18.5%)	----

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

Species	Stage	Test Substance	Dose (g as/ha)	Endpoint	Effect	Annex VI Trigger
Typhlodromus pyri	Protonymph	Methomyl 20 SL aged on grape leaves	22.5 33.75 450	Mortality Reproduction Mortality Reproduction ratio Mortality Reproduction ratio	Fresh residues 0% Not available 5.4% 1.06 (Control = 7.7 eggs/female) 7-d old residues 3.3% 0.79 (Control = 9.2 eggs/female)	----
Chrysoperla carnae	Larvae	Methomyl 20 SL aged on grape leaves	1250 x 3	Mortality Reproduction	0-d = 100% 4-d = 42.3% 7-d = -3.6% 14-d = 20.0% 21-d = 0.0% 4-d = 8.3% 7-d = 17.0% 14-d = 5.3% 21-d = 27.1%	----
Orius laevigatus	Adult	Methomyl 20 SL aged on grape leaves	450 x 2	Mortality Reproduction	0-d = 100% 5-d = 9% 10-d = -18% 20-d = 13% 5-d = 20% 10-d = 0% 20-d = -17%	----

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

Species	Stage	Test Substance	Dose (g as/ha)	Endpoint	Effect	Annex VI Trigger
Poecilus cupreus	Adult	Methomyl 20 SL aged on soils	720	Mortality	1-d = 0.0% 5-d = 0.0% 10-d = 3.3%	----
				Food consumption	1-d = -2.6% 5-d = -4.2% 10-d = -2.4%	
			2880	Mortality	1-d = 90.0% 5-d = 26.7% 10-d = 36.7%	
				Food consumption	1-d = 56.6% 5-d = -0.8% 10-d = -0.4%	
Aleochara bilineata	Adult	Methomyl 20 SL aged on soils	720	Mortality	1-d = 21.3% 5-d = 3.8% 10-d = 0.0%	----
				Reproduction	1-d = 42.0% 5-d = 5.3% 10-d = -3.9%	
			2880	Mortality	1-d = 88.8% 5-d = 25.0% 10-d = 2.5%	
				Reproduction	1-d = 99.8% 5-d = 94.5% 10-d = 79.4%	

Field or semi-field tests

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

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

Acute toxicity ‡	LC_{50} = 38.5 mg a.s./kg based on active substance LC_{50} = 19 mg methomyl/kg based on metabolite LC_{50} = 90.3 mg a.s./kg based on 'RPA 62980 I' (similar to 'Larvin')
Reproductive toxicity ‡	NOEC = 2 mg a.s./kg based on active substance

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

Application rate (kg as/ha)	Crop	Toxicity endpoint	Time-scale	TER	Annex VI Trigger
Thiodicarb					
0.375 x 2 PEC of 0.237 mg a.s/kg	Grapevines	LC_{50} = 38.5 mg a.s./kg	14 d	162.4	10
0.375 x 2 PEC of 0.237 mg a.s./kg	Grapevines	NOEC 2.0 mg a.s./kg	56 d	8.4	5
Methomyl					
0.375 x 2 PEC of 0.218 mg methomyl/kg	Grapevines	LC_{50} = 19 mg methomyl/kg	14 d	87.2	10

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

Nitrogen mineralization ‡	Effects < 25% at 1 mg a.s./kg soil Effects < 25% at 10 mg a.s./kg soil (based on thiodicarb)
Carbon mineralization ‡	Effects < 25% at 1 mg a.s./kg soil Effects < 25% at 10 mg a.s./kg soil (based on thiodicarb)

Non target terrestrial plants (Annex IIA point 8.6. Annex IIIA, point 10.8)

Seedling emergence	No effect on 9 monocotyledon spp and 10 dicotyledon spp. at 950 g a.s./ha (based on 'Larvin')
Seedling growth	No effect on 9 monocotyledon spp. and 10 dicotyledon spp. at 950 g a.s./ha (based on 'Larvin')

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

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N; Dangerous for the environment R50 Very toxic to aquatic organisms) R53 May cause long term adverse effects in the aquatic environment) S60 This material and its container must be disposed of as hazardous waste S61 Avoid release to the environment. Refer to special instructions/Safety Data Sheet

Skipper

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

Acute toxicity to mammals	LD_{50} = 50 mg thiodicarb/kg bw/d (rat)
Acute toxicity to birds	LD_{50} = 2023 mg thiodicarb/kg bw/d (bobwhite quail) LD_{50} = 24.2 mg methomyl/kg bw/d (bobwhite quail)
Dietary toxicity to birds	LC_{50} > 5620 ppm thiodicarb (bobwhite quail and mallard duck) LC_{50} = 3952 ppm methomyl (658 mg/kg bw/day) (mallard duck)
Reproductive toxicity to birds	NOEC = 500 ppm thiodicarb (mallard duck) NOEC (parental) = 150 ppm methomyl (mallard duck) NOEC (reproductive) = 500 ppm methomyl (mallard duck)
Reproductive toxicity to mammals	NOEC = 100 ppm thiodicarb (rat)

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
Thiodicarb					
Pellet consumption					
0.2 x 3	Cereals	Granivorous bird	Acute	0.17	10
0.2 x 3	Cereals	Granivorous bird	Short-term	0.14	10
0.2 x 3	Cereals	Granivorous bird	Long-term	0.0125	5

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.2 x 3	Cereals	Small granivorous mammal	Acute	0.00417	10
0.2 x 3	Cereals	Small granivorous mammal	Long-term	0.0025	5
Earthworm consumption					
0.2 x 3	Cereals	Earthworm eating bird	Acute	156	10
0.2 x 3	Cereals	Earthworm eating bird	Short-term	>312	10
0.2 x 3	Cereals	Earthworm eating bird	Long-term	28	5
0.2 x 3	Cereals	Earthworm eating mammal	Acute	3.9	10
0.2 x 3	Cereals	Earthworm eating mammal	Long-term	5.6	5
Vegetation consumption					
0.2 x 3	Cereals	Herbivorous bird	Acute	210729	10
0.2 x 3	Cereals	Herbivorous bird	Short-term	140500	10
0.2 x 3	Cereals	Herbivorous bird	Long-term	12500	5
0.2 x 3	Cereals	Herbivorous mammal	Acute	5208	10
0.2 x 3	Cereals	Herbivorous mammal	Long-term	2500	5
Methomyl					
Pellet consumption					
0.2 x 3	Cereals	Granivorous bird	Acute	0.037	10
0.2 x 3	Cereals	Granivorous bird	Short-term	4.3	10
0.2 x 3	Cereals	Granivorous bird	Long-term (reproductive)	0.543	5
0.2 x 3	Cereals	Granivorous bird	Long-term (parental)	0.163	5
Earthworm consumption					
0.2 x 3	Cereals	Earthworm eating bird	Acute	2.1	10

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.2 x 3	Cereals	Earthworm eating bird	Short-term	241	10
0.2 x 3	Cereals	Earthworm eating bird	Long-term (reproductive)	30.5	5
0.2 x 3	Cereals	Earthworm eating bird	Long-term (parental)	9.2	5
Vegetation consumption					
0.2 x 3	Cereals	Herbivorous bird	Acute	2688	10
0.2 x 3	Cereals	Herbivorous bird	Short-term	106811	10
0.2 x 3	Cereals	Herbivorous bird	Long-term (reproductive)	13513.5	5
0.2 x 3	Cereals	Herbivorous bird	Long-term (parental)	4054	5

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 test substance/L)
Laboratory tests				
Lepomis macrochirus	thiodicarb	96 h	Mortality LC_{50}	1.4
Pimephales promelas	thiodicarb	35 d	Growth NOEC	0.025
Daphnia magna	thiodicarb	48 h	Mortality EC_{50}	0.027
Daphnia magna	thiodicarb	21 d	Reproductive NOEC	0.009
Chironomus riparius	thiodicarb	28 d	Reproductive NOEC	0.080
Pseudokirchneriella subcapitata	thiodicarb	96 h	Biomass EC_{50}	18
Lepomis macrochirus	methomyl	96 h	Mortality LC_{50}	0.62
Daphnia magna	methomyl	48 h	Mortality EC_{50}	0.017
Daphnia magna	methomyl	21 d	Reproductive NOEC	0.0016
Pseudokirchneriella subcapitata	methomyl	72 h	Biomass EC_{50}	94

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

Microcosm or mesocosm tests
Not required.

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
Drainflow - Methomyl						
0.2	Cereals	*Lepomis macrochirus*	96 h	0	3875	100
0.2	Cereals	*Daphnia magna*	48 h	0	106.25	100
0.2	Cereals	*Pseudokirchneriella subcapitata*	72 h	0	587500	10
0.2 (based on thiodicarb)	Cereals	*Pimephales promelas*	35 d	0	156	10
0.2	Cereals	*Daphnia magna*	21 d	0	10	10

For drainflow and groundwater, thiodicarb is not considered to be an issue.

For groundwater, methomyl is considered to be a Member State issue due to exceedences in 2 out of the 9 scenarios.

Bioconcentration

Bioconcentration factor (BCF) ‡	6.3
Annex VI Trigger for the bioconcentration factor	100 for compound not readily biodegradable
Clearance time (CT_{50}) (CT_{90})	12 +/- 0.81 days Not determined

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

Acute oral toxicity ‡	48 h LD_{50} = 0.153 µg a.s./bee based on active substance
Acute contact toxicity ‡	48 h LD_{50} = 3.1 µg a.s./bee based on active substance

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

Not calculated for 'Skipper' due to the application regime.

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

Field or semi-field tests. None conducted.

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

Species	Stage	Test Substance	Dose (g as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests – extended (I) The trigger value in Directive 97/57/EC is 30% (ESCORT2 refers to values of 50% for extended laboratory studies)						
Poecilus cupreus	Adult	Skipper	200	Mortality Consumption	Day 15 = 73.33% Day 29 = 76.67% 1.44 pupae/day (control = 1.23)	----
Aleochara bilineata	Adult	Skipper	200	Parasitic capacity	70.1% (control = 69.2%)	----
Laboratory tests – extended (II) The trigger value in Directive 97/57/EC is 30% (ESCORT2 refers to values of 50% for extended laboratory studies)						
Poecilus cupreus	Adult	Methomyl 20 SL aged on soils	720 2880 	Mortality Food consumption Mortality Food consumption	1-d = 0.0% 5-d = 0.0% 10-d = 3.3% 1-d = -2.6% 5-d = -4.2% 10-d = -2.4% 1-d = 90.0% 5-d = 26.7% 10-d = 36.7% 1-d = 56.6% 5-d = -0.8% 10-d = -0.4%	----

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

Species	Stage	Test Substance	Dose (g as/ha)	Endpoint	Effect	Annex VI Trigger
Aleochara bilineata	Adult	Methomyl 20 SL aged on soils	720	Mortality	1-d = 21.3% 5-d = 3.8% 10-d = 0.0%	----
				Reproduction	1-d = 42.0% 5-d = 5.3% 10-d = -3.9%	
			2880	Mortality	1-d = 88.8% 5-d = 25.0% 10-d = 2.5%	
				Reproduction	1-d = 99.8% 5-d = 94.5% 10-d = 79.4%	

Field or semi-field tests. None conducted.

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

Acute toxicity	LC_{50} = 19 mg methomyl/kg based on metabolite
Reproductive toxicity	NOEC = 2 mg a.s./kg based on active substance NOEC = 1.5 mg methomyl/kg based on methomyl

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

Application rate (kg as/ha)	Crop	Toxicity endpoint	Time-scale	TER	Annex VI Trigger
Thiodicarb - Exposure from the soil					
0.2 x 3 PEC of 0.372 mg a.s./kg	Cereals	NOEC 2.0 mg a.s./kg	56 d	5.4	5

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

Application rate (kg as/ha)	Crop	Toxicity endpoint	Time-scale	TER	Annex VI Trigger
Methomyl – Exposure from the soil					
0.2 x 3 PEC of 0.584 mg methomyl/kg	Cereals	LC_{50} = 19 mg methomyl/kg	14 d	32.5	10
0.2 x 3 PEC of 0.584 mg methomyl/kg	Cereals	NOEC = 1.5 mg methomyl/kg	56d	2.57	5

Acute risk to earthworms from the pellet could not be assessed.

Effects on other soil macro-organisms

Unable to resolve at this time.

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

Nitrogen mineralization	Effects < 25% at 1 mg a.s./kg soil Effects < 25% at 10 mg a.s./kg soil (based on thiodicarb)
Carbon mineralization	Effects < 25% at 1 mg a.s./kg soil Effects < 25% at 10 mg a.s./kg soil (based on thiodicarb)

Non target terrestrial plants (Annex IIA point 8.6. Annex IIIA, point 10.8)

Seedling emergence	No effect on 9 monocotyledon spp and 10 dicotyledon spp. At 0.4 kg a.s./ha (based on 'Skipper' spray applications)
Seedling growth	No effect on 9 monocotyledon spp. and 10 dicotyledon spp. At 0.4 kgg a.s./ha (based on 'Skipper' spray applications)

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N; Dangerous for the environment R50 Very toxic to aquatic organisms, R53 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

S60	This material and its container must be disposed of as hazardous waste
S61	Avoid release to the environment. Refer to special instructions/Safety Data Sheet

‡ 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
ER_{50}	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