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

pirimicarb

finalised: 10 August 2005

SUMMARY

Pirimicarb 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 pirimicarb in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 4 November 2003. Following a quality check on the DAR, the peer review was initiated on 4 December 2003 by dispatching the DAR for consultation of the Member States and the sole applicant Syngenta. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting on 25 May 2004. Remaining issues as well as further data made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in September and October 2004.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 19 July 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 as proposed by the notifier which comprises broadcast spraying to control aphids in wheat at application rate up 0.21 kg pirimicarb per hectare. Pirimicarb can be used only as insecticide. The representative formulated product for the evaluation was "Pirimor" ("YF7904B"), a water dispersible granule (WG), registered under different trade names in Europe.

[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 finalised residue definition. Only single methods for determine 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.

Mammalian toxicity during oral and inhalatory exposure is high and pirimicarb is a skin sensitizer, proposal for classification is T; R23/25 "Toxic by inhalation and if swallowed" and R43 "May cause sensitization by skin contact". Main effects observed during short term exposure were reduction in cholinesterase activity and haematological effects. Due to the consistent effects on haematological parameters at relatively low dose levels throughout the studies the proposal for classification is R48/22 "Danger of serious damage to health by prolonged oral exposure"
There is no genotoxic potential for pirimicarb. However, in the mouse indications of a possible increase of pulmonary tumours were observed which were outside the upper historical control range. The experts' meeting could not come to an agreement whether on classification was required or not. Therefore, a question mark is added to the risk phrase and Xn; R40? is proposed "Limited evidence of a carcinogenic effect". Neither reproductive or developmental toxicity nor neurotoxicity was observed.
The acceptable daily intake (ADI) and acceptable operator exposure level (AOEL) is 0.035 mg/kg bw/day and the acute reference dose (ARfD) is 0.1 mg/kg bw, the safety factor of 100 is used.
The estimated operator exposure according to the German model is below the AOEL without PPE. According to the UK-POEM gloves and respiratory personal equipment (RPE) is needed during mixing and loading and coveralls and gloves when handling contaminated surfaces. Thus, it would be appropriate to include the use of gloves and RPE due to the sensitizing properties of pirimicarb and due to the fact that it is toxic during acute oral and inhalation exposure.

The metabolism of pirimicarb has been studied on wheat and supportive information was provided for 3 other crops. The residues of concern in wheat were found to be pirimicarb itself and 2 carbamate metabolites with similar or higher level of toxicity, R34836[3] and R34885[4]. In other crops, another metabolite, R35140[5] was also present. For the use on grain, the proposed residue definition (sum of pirimicarb, R34836 and R34885 expressed as pirimicarb) for monitoring is efficient to protect adequately the safety of the consumers.
No concern was identified for rotational and succeeding crops.
The metabolism of pirimicarb in ruminant and poultry is extensive and the use of pirimicarb in wheat does not lead to the presence of the active substance or its carbamate metabolites in edible animal tissues. A residue definition consisting of pirimicarb only in animal tissues is proposed, although the

[3] R34836: 5,6-dimethyl-2-(methylamino)pyrimidin-4-yl dimethylcarbamate
[4] R34885: 5,6-dimethyl-2-(methylformamido)pyrimidin-4-yl dimethylcarbamate
[5] R35140: 2-amino-5,6-dimethylpyrimidin-4-yl dimethylcarbamate

monitoring of this compound when used under the proposed representative use does not provide value in term of consumer safety.
The intake calculations for acute and long term exposures do not show any concern for the safety of the consumer.

Under aerobic conditions, transformations of pirimicarb in soil yields the major metabolites R34885, R31805[6] and R34865[7]. Metabolite R34836 does not reaches the 10 % AR in soil but was considered relevant because contains the intact carbamate toxophore. Mineralization of pirimicarb was low and unextractable residues accounted for a maximum of 14.9 % AR after 84 d. Under dark anaerobic conditions only metabolite R31805 was found at amounts above 10 % AR.
Photolysis in soil may contribute to the environmental degradation of pirimicarb. Metabolite R34836 was the only photoproducts found at amounts above 10 % AR.
Dissipation of pirimicarb under field conditions was investigated in two field studies in California (USA) and Germany (EU). In the California field study the metabolite R35140 containing the carbamate moiety was identified at average levels of 1.98 % of applied amount. Due to the fact that it contains the carbamate moiety it is considered as a relevant metabolite for soil compartment.
Pirimicarb is medium to high persistent in soil ($DT_{50\ 20°C\ FMOC}$ = 29 – 143 d).
After the experts' meeting on fate and behaviour in the environment (EPCO 12, September 2004), RMS received an evaluation document from one MS summarizing the results of three laboratory degradation studies performed in the 1970s that was included in Addendum 4 to the DAR (December 2004). Since the original reports are still not available for evaluation these results are not considered in this conclusion and the confirmatory data requirement is maintained for these studies. It is the opinion of the RMS that, according the summary available to them, the trend for longer DT_{50} at lower pH is not fully consistent and that no evidence of pH effects are observed in the aqueous hydrolysis study (pirimicarb stable at pH 5-9). However, at least degradation in an additional soil would be necessary to fulfil data requirement as given in 91/414/EEC Annex II 7.1.1.2.1. since studies in only three soils are available. Experts meeting considered that field studies may qualitatively indicate a shorter persistence in field under bare soil conditions but no reliable DT_{50} may be obtained from them. Therefore, if the studies to be submitted with respect to the data requirement set by the evaluation meeting (see above) are finally not found acceptable to cover this data gap new data may need to be generated and provided.
Metabolite R34836 is low to medium persistent ($DT_{50\ 20°C}$ = 7 d – 90 d), R31805 is moderately persistent ($DT_{50\ 20°C}$ = 33 d – 38 d) and R34865 is moderate to medium persistent ($DT_{50\ 20°C}$ = 37 d – 78 d). Metabolite R34885 appears to be moderately persistent in soil ($DT_{50\ 20°C}$ = 14 d – 31 d).
Photolysis in soil may contribute to pirimicarb dissipation according laboratory soil photolysis.
Initially, RMS used field half life to calculate PEC soil. The experts meetings did not accept this because field studies were performed in bare soil and representative uses imply application to fully developed crops. The contribution of photolysis may have been overestimated in the bare soil studies with respect to the lower irradiation in the cropped field. Therefore, worst case laboratory DT_{50} = 150

[6] R31805: 2-dimethylamino-5,6-dimethylpyrimidin-4-ol
[7] R34865: 5,6-dimethyl-2-(methylamino)pyrimidin-4-ol

d was agreed for PEC soil calculations. New PEC soil calculations may be found in the Addendum to the DAR (December 2004).

The results of batch adsorption/desorption studies indicate that pirimicarb is low to high mobile, R34836 could be classified as slightly to very high mobile, R34885 low to high mobile R31805 immobile to high mobile and R34865 immobile to medium mobile. R31805 appears to present stronger adsorption in more acidic soils. Experts meeting considered that a dependence of the K_{foc} values on the soil clay content could be deduced and may need to be considered by MS in their assessments.

Pyrimicarb was found to be stable to hydrolysis at environmental relevant pH 5 to 9.

Photochemical degradation of pirimicarb in water under mid-European conditions is relatively rapid. Three major photochemical metabolites were identified: R34885, R31805 and R16210[8].

Experts meeting considered pirimicarb to be not ready biodegradable based on water sediment study.

In water sediment systems, pirimicarb partitions slowly from the water to the sediment. Degradation of pirimicarb in the sediment is very limited. Pirimicarb remained as the major component in both the water and the sediment. Mineralization was very low.

Surface water risk assessment presented in the DAR is based on spray drift route of entry to surface water and considered photolysis in water (DT_{50} < 1d) as the main route of dissipation.

The experts meeting agreed that whereas photolysis may play an important role to the dissipation of pirimicarb in certain environmental conditions, risk assessment based on a non-photolysis situation must be considered for EU evaluation. Therefore, PECsw were recalculated based on the longest first order dissipation half life (DT_{50} = 55d) for the water phase of the dark water/sediment system (Addendum 4, December 2004).

Potential surface water contamination due to drainage and run off were not considered in the DAR. These routes may not be precluded and surface water risk assessment may not be considered complete without addressing them.

The experts meeting identified potential for accumulation of pirimicarb into the sediment. Since no reliable half-life in the sediment may be obtained from the available water sediment study, a reasonable worst-case estimation was done by using DT_{50} = 335 d from the anaerobic soil degradation study. This value was used to calculate an accumulated PEC_{sed} = 29 µg / kg (Addendum 4, December 2004). However, as for the PECsw calculations this value only incorporates potential loadings through spray drift.

The potential leaching of pirimicarb and its metabolites R34836, R34885, R31805, R34865 to ground water was simulated with FOCUS PELMO 3.3.2 for the nine FOCUSgw scenarios. The resulting concentration for all the nine scenarios were below 0.001 µg / L. Soil metabolite R35140 identified in some field studies has not been assessed for potential ground water contamination. EFSA is of the opinion that it is very unlikely that the trigger of 0.1 µg / L would be exceeded by this metabolite. However, it needs to be properly addressed due the fact that it is more acutely toxic than the parent pirimicarb.

[8] R16210: 1,1-dimethylguanidine

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

If exposure is calculated according to EPPO (1992), a high acute risk to birds from the use of pirimicarb was identified in the first tier risk assessment. The EPCO experts' meeting on ecotoxicology (EPCO 13) decided to seek an opinion of EFSA's Panel on Plant Health, Plant Protection Products and their Residues (PPR) on the principles used to refine this risk. The PPR Panel assessed the risk to birds feeding on insects in cereal fields after treatment with pirimicarb. Based on the results of this assessment, the PPR Panel is of the opinion that even at the upper limit of credible exposures, birds feeding on insects in the field are unlikely to achieve a lethal dose of pirimicarb[9].
The short and long term risk to birds can be regarded as low if exposure is calculated according to EPPO (1992). EFSA made a first tier risk assessment available according to SANCO/4145/2000 which confirms the high acute risk to birds but also indicates a long term risk to birds. Therefore, EFSA proposes a data requirement for the notifier to submit a refinement of the long term risk to birds if the risk is assessed according to the latest guidance document (SANCO/4145/2000). For the acute risk to birds see opinion of the PPR Panel discussed above.
The acute and long term risk to mammals can be regarded as low if exposure is calculated according to EPPO (1992) and also if exposure is calculated according to SANCO/4145/2000.
The risk to aquatic organisms can be considered as high if the risk assessment is based on the standard toxicity studies with *Daphnia magna* without the presence of sediment. Risk mitigation measures need to be taken into account at MS level to address this risk. The experts' meeting (EPCO 13) decided to await the outcome of the opinion of EFSA's PPR Panel on dimoxystrobin[10] concerning the use of a study with the presence of sediment to refine the risk. Any further refinements of the risk to aquatic organisms based on studies in the presence of sediment should be performed in accordance with the opinion of the Scientific Panel on Dimoxystrobin.
The experts' meeting (EPCO 13) considered the risk to bees and non target arthropods as addressed based on the available data.
The risk to soil non-target micro-organisms from pirimicarb and the metabolites R31805 and R34865 is considered to be low. It is noted by EFSA that no studies with the soil metabolites R35140, R34885 and R34836 are available. Therefore, EFSA proposes that a study or at least a solid argumentation regarding the effects of these metabolites on soil non-target micro-organisms should be made available. The need for these data was not discussed at an EPCO experts' meeting.
The risk to earthworms, soil non-target macro-organisms, non-target terrestrial plants and biological methods of sewage treatment is considered to be low.

Key words: pirimicarb, peer review, risk assessment, pesticide, insecticide

[9] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR) on a request from EFSA related to the evaluation of pirimicarb. *The EFSA Journal* (2005) 240, 1-21.
[10] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR) on a request from EFSA related to the evaluation of dimoxystrobin. *The EFSA Journal* (2005) 178, 1-45.

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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. Pirimicarb 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 pirimicarb, hereafter referred to as the draft assessment report, to the EFSA on 4 November 2003. 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 4 December 2003 to the Member States and the main notifier Syngenta 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 25 May 2004 on data requirements to be addressed by the main 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 experts' meetings organised on behalf of the EFSA by the Pesticide Safety Directorate in York, United Kingdom in September and October 2004. 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 19 July 2005 leading to the conclusions as laid down in this report.

Following the consultation of technical experts a question relating to the acute risk assessment for birds was forwarded to the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR) which was addressed by an opinion adopted on 6 July 2005.

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 1 July 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. 1-2 of 9 August 2005).

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

Pirimicarb is the ISO common name for 2-dimethylamino-5,6-dimethylpyrimidin-4-yl dimethylcarbamate (IUPAC).

Pirimicarb belongs to the class of dimethylcarbamate insecticides. Pirimicarb acts by inhibiting the acetylcholinesterase enzyme, which results is an uncontrolled series of nerve impulses.
The representative formulated product for the evaluation was "Pirimor" ("YF7904B"), a water dispersible granule (WG), registered under different trade names in Europe.

The evaluated representative uses as insecticide comprises broadcast spraying to control aphids in wheat at application rate up 0.21 kg pirimicarb per hectare. Pirimicarb can be used only as insecticide.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of pirimicarb as manufactured is proposed to be not less than 950 g/kg. The specification should be regarded as provisional, because clarification is needed to confirm the proposed levels in the technical material with respect to pirimicarb and the impurities. The technical material contains no relevant impurities.
At the moment no FAO specification exists.

Beside this, the assessment of the data package on the identity, physical, chemical and technical properties of pirimicarb or the respective formulation revealed no particular area of concern, but some data gaps have been identified. Data on boiling point and partition coefficient are missing or need to be clarified. Also adequate analytical methods are available for the determination of pirimicarb in the technical material and in the representative formulation.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

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

Adequate methods are available to monitor all compounds given in the respective finalised residue definition, i.e. pirimicarb, desmethyl pirimicarb (R34836[11]) and desmethylformamido pirimicarb (R34885[12]) in food of plant origin; pirimicarb in surface water and air.
For the moment the residue definitions for soil and ground water are not finalised. In case of soil a validated analytical method is available only for the determination of metabolite R34836 but not for R4885 and R35140. For ground water no method is available for the determination of residues of metabolite R35140.
An analytical method for food of animal origin is not required due to the fact that no MRL is proposed (see 3.2 and 3.4).

Concerning some missing clarification in the DAR with respect to the residue analytical methods, EFSA would like to clarify the following: It should be noted that for food of plant origin no specific enforcement is available to distinguish between desmethyl pirimicarb (R34836) and desmethylformamido pirimicarb (R34885), because they are quantified by the same analyte. Furthermore, the method was only validated by fortification with pirimicarb and R34836.

The methodologies used are GC with PN, fluorescence or MS detection or HPLC with UV, MS or MS/MS detection. EFSA is of the opinion that for confirmatory purposes (food of plant origin), the

[11] R34836: 5,6-dimethyl-2-(methylamino)pyrimidin-4-yl dimethylcarbamate
[12] R34885: 5,6-dimethyl-2-(methylformamido)pyrimidin-4-yl dimethylcarbamate

LC-MS/MS method of Wright (1998) given in the dossier, but not mentioned in the DAR can be used. Due to the nature of the residues multi-residue methods like the German S19 or the Dutch MM1 are not applicable.

The discussion in the experts' meeting on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material and some physical and chemical properties of pirimicarb and some open points with respect to the residue analytical methods in particular for food of animal origin and methods for the determination of impurities.

A recently submitted study, regarding the determination of the boiling point/temperature of decomposition was not yet assessed by the RMS. Some of the needed clarification with respect to the applicability of a multi-residue method for food of plant origin, the method for air and the method for the determination of two significant impurities are given at the moment only in the evaluation table [rev. 1-0 (11.07.2005)].

2. Mammalian toxicology

Pirimicarb is an insecticide (aphicide) that acts by inhibiting the acetyl cholinesterase activity. In October 2004 pirimicarb was discussed at the EPCO experts´ meeting (EPCO 14) with respect to questions in relation to mammalian toxicology.

2.1 Absorption, distribution, excretion and metabolism (Toxicokinetics)

Pirimicarb is rapidly and nearly completely absorbed, > 80% (59 – 72% via urine and 24% via biliary excretion). The excretion is also rapid, 60-70% within 24 hours mainly in urine. It is widely distributed and the highest concentration was found in the liver. There was no evidence of accumulation. Pirimicarb is extensively metabolised and the major pathway is involving a loss of the carbamate moiety to produce a range of substituted hydroxypyrimidines. There were numerous of metabolites evident, see 2.8.

2.2 Acute toxicity

The oral toxicity is high i.e. oral LD_{50} around 150 mg/kg bw/day as well as during inhalatory exposure LC_{50} around 0.9 mg/L air. However, the toxicity via dermal route was low, the LD_{50} >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; R23/25 Toxic by inhalation and if swallowed" and R43 "May cause sensitization by skin contact".

2.3 Short term toxicity

The short term effects of pirimicarb were studied in two 8-week dietary studies and one 90-day study in the rat, two 90-day studies in the dog, one 16 week study in foxhounds, one 1-yr study in the dog and one 2-yr study in the dog. The 1-yr dog study is from 1997 while the other studies are of old date

(1968 to 1978) and some of them according to a limited protocol and not in full compliance with GLP.

The main effects observed were reduction in cholinesterase activity and haematological effects. Anaemia was observed at the dose level of 4 mg/kg bw/day and above in the 13-16 weeks dog studies. However, complete recovery was demonstrated where reversibility was investigated. In the 1-year dog study anaemia was also observed as well as inhibition of brain and erythrocyte cholinesterase activity and tremors although sampling time was late i.e. 22 hours after dosing.

The effects and setting of a relevant short term NOAEL was discussed at the expert's meeting. It was debated whether NOAEL of 2 mg/kg bw/day based on bone marrow changes at 4 mg/kg bw/day from the 90-day dog study should be used. However, it was agreed at the meeting that the NOAEL of 3.5 mg/kg bw/day from recent 1-yr dog study could be the overall NOAEL for short term studies. This was based on the fact that the cholinesterase effects were similar to those observed in the 90-days dog study i.e. no progression was evident.

Thus, the relevant oral NOAEL is 3.5 mg/kg bw/day from the 1-year dog (Horner, 1998). **It was proposed to classify pirimicarb as R48/22 "Danger of serious damage to health by prolonged oral exposure" due to the consistent effects on haematological parameters at relatively low dose levels throughout the studies.**

The relevant dermal NOAEL is 200 mg/kg bw/day based on reduced brain cholinesterase activity at 1000 mg/kg bw/day. However, it should also be noted that the sampling time was delayed to 18-24 hrs after last topical application.

No studies were submitted on repeated inhalation.

2.4 GENOTOXICITY

In the DAR the genotoxic properties of pirimicarb were studied in a battery consisting of four *in vitro* studies (of which two Ames tests) and three *in vivo* studies. The purity was between 97 and 98% which is higher than the minimum purity specified however there are no relevant impurities of concern. Pirimicarb was negative in the Ames tests, but positive in the mouse lymphoma test in the presence of metabolic activation. On the other hand, pirimicarb was negative in all *in vivo* tests. The overall conclusion is that there is no genotoxic potential for pirimicarb.

2.5 LONG TERM TOXICITY

One recent long term toxicity study in the rat and two in the mouse were submitted in the dossier. However, the RMS was aware of three other older (1975) studies in the rat which were evaluated in the UK pirimicarb review (2001). The RMS presented a brief summary of these studies as well in the DAR. The studies were of old date and were considered as inadequate and not in compliance with guidelines. Although, it should be noted that chronic respiratory infection was reported in all these studies and that in one of the studies lung tumours and in another mammary gland fibroadenoma were observed. The mammary gland fibroadenoma was observed at higher dose levels than administered in the more recent study in the rat (performed in 1989) where the administered dose levels was approximately 30% of the LD_{50}, and the survival rate was generally low even in the control group.

In the modern study no carcinogenic potential was evident at any doses, top dose 750 ppm i.e. 37.3 and 47.7 mg/kg bw/day in males and females, respectively. However, a high mortality rate was evident. The NOAEL was determined to be 3.7 and 4.7 mg/kg bw/day in males and females, respectively based on reduced bw, food consumption, clinical chemistry and liver and kidney effects.

Two studies were performed in the mouse. In the first study a high mortality rate was evident as well as respiratory diseases. Although there were significant deficiencies in the study there were indications of a possible increase of pulmonary tumours. Further on, in the second study there was an increased incidence of pulmonary adenomas in the top dose (700 ppm i.e. 93.7 and 130.3 mg/kg bw/day for males and females, respectively) which was outside the upper historical control range. The RMS considered these effects to be treatment related.

During the Experts' meeting the proposal for classification was discussed. The relevance of lung tumours for humans was questioned. The occurrence of tumours in the used strain of mouse is very rare. This fact in combination with the low survival rate in the recent study lead to uncertainties regarding the conclusion and the meeting could not come to an agreement whether this was required or not. **Therefore, a question mark is added to the risk phrase and Xn; R40? is proposed "Limited evidence of a carcinogenic effect" and the final decision is to be made by ECB.**

2.6 REPRODUCTIVE TOXICITY

One multigeneration study in the rat in order to determine the reproductive effects of pirimicarb is presented in the DAR. There were no direct effects on reproductive performance or fertility observed. The parental NOAEL was 200 ppm i.e. 21.7 and 22.5 mg/kg bw/day based on reduced body weight gain and food consumption. The relevant NOAEL for reproduction was > 750 ppm i.e. 81.8 and 83.8 mg/kg bw/day in males and females, respectively.

In order to examine teratogenic or developmental effects of pirimicarb one study in the rat and one in the rabbit were submitted in the dossier and evaluated in the DAR. Skeletal effects were seen in the foetuses whereas reduced body weight and food intake were major maternal effects in both the rat and the rabbit. It is concluded that pirimicarb did not induce teratogenic or foetotoxic effects at non-maternally toxic doses. The NOAEL for maternal and foetal/developmental effects in the rat is 25 mg/kg bw/day.
The relevant maternal NOAEL and foetal/developmental NOAEL is from the rabbit which is 10 mg/kg bw/day based on similar effects as in the rat.

2.7 NEUROTOXICITY

Neurotoxicological studies were performed and they are reported under other toxicological studies in the DAR (see B.6.8).
In an acute neurotoxicity study in the rat reduced brain acetyl cholinesterase activity was observed at 110 mg/kg bw, transient clinical signs reflecting cholinergic effects were seen at dose levels of ≥ 40 mg/kg bw and ≥ 10 mg/kg bw/day in males and females, respectively. The NOAEL was considered to

be 10 mg/kg bw for both sexes based on the overall reductions in motor activity (>10%) and effects on cholinesterase at 40 mg/kg bw and up.

No sign of neurotoxicity was observed during short term exposure in the rat and the NOAEL was 77.1 and 84.4 mg/kg bw/day for males and females. The NOAEL for general systemic toxicity was 5.6 and 6.6 mg/kg bw/day based on decreased body weight and food utilization.

Pirimicarb is a carbamate and not an organo phosphorus compound and there was no evidence of an effect on brain neuropathy target esterase (NTE) activity in neurotoxicity studies. Therefore, no studies on delayed neurotoxicity are available.

2.8 FURTHER STUDIES

Metabolism

The *in vitro* metabolism (rat hepatocytes) of pirimicarb and two of its known plant metabolites R34885 and R34836 was investigated in order to propose a qualitative comparison of mammalian metabolism of pirimicarb and the metabolites. The metabolic conversion of the metabolites was found to have a similar pattern as pirimicarb.

Acute toxicity studies on metabolites

Acute toxicity studies were performed on several metabolites. The metabolites R35140, R34885 and R34836 all more toxic or in the same range as pirimicarb, see table below.

Metabolite	LD_{50} (mg/kg bw)
R31805[13]	800-1600
R31680[14]	> 2500
R34836	200-400
R34865[15]	> 2000
R34885	50-100
R35140[16]	79
guanidine hydrochloride	1105
methyl guanidine sulphate	1105
dimethyl guanidine hydrochloride[17]	1445

[13] R31805: 2-dimethylamino-5,6-dimethylpyrimidin-4-ol
[14] R31680: 2-amino-5,6-dimethylpyrimidin-4-ol
[15] R34865: 5,6-dimethyl-2-(methylamino)pyrimidin-4-ol
[16] R35140: 2-amino-5,6-dimethylpyrimidin-4-yl dimethylcarbamate
[17] 1,1-dimethylguanidine hydrochloride

Repeated dose studies on metabolites

R34836 was tested in the three older (around 1970) rat studies. Clinical signs indicative of cholinesterase inhibition were noted. However, no effects on erythrocyte or brain cholinesterase were recorded probably due to inadequate technology applied. Effects on plasma cholinesterase (25%) were observed at 100 mg/kg bw/day. The dose levels at which the metabolite inhibits plasma cholinesterase is similar to that of pirimicarb. A NOAEL of 5 mg/kg bw/day based on mortality occurring at 25 mg/kg bw/day is set.

Two studies in the rat, also of older date, were evaluated on the metabolite R34885. The dose level at which the metabolite inhibits plasma cholinesterase activity is similar to that of pirimicarb. The NOAEL is 50 mg/kg bw/day (highest dose tested).

Genotoxicity studies on metabolites

The hydroxypyrimidine metabolite R31805 is converted *in vivo* to R34865 and thus R34865 can be said to be adequately tested within the studies in the rat on R31805. The NOAEL was 19.5 and 7.3 mg/kg bw/day for males and females, respectively based on clinical chemistry changes in the liver. R31805 was negative in the Ames test but demonstrated to be mutagenic in the mouse lymphoma test whereas not in the study with human lymphocytes. R31805 did not induce DNA repair as determined with UDS test in the rat liver *in vivo*. R34865 was found to be negative (both with and without S9-mix) in a recently performed Ames test. However, it was found to be mutagenic *in vitro* (mouse lymphoma cells) at cytotoxic concentration. R34865 was not clastogenic in human lymphocytes.

Summary of metabolites of toxicological relevance

With respect to acute toxicity it can be concluded that the metabolites R35140, R34885 and R34836 all more toxic or in the same range as pirimicarb. No genotoxicologal studies on either of the metabolites are available. Thus, they are to be considered as toxicologically relevant.

2.9 MEDICAL DATA

Reports from plant employees (monitoring data 1969-1973) exposed for pirimicarb and pirimicarb containing products describe effects such as reduced plasma and erythrocyte cholinesterase activities, usually without clinical symptoms of cholinergic toxicity. However, up to 40% cholinesterase (whole blood) inhibition may occur without evidence of systemic symptoms. Recovery is rapid and complete.

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

ADI and AOEL

The Rapporteur member state proposed to set the ADI as well as AOEL on the NOAEL of 3.5 mg/kg bw/day from the 1-year dog study using the safety factor of 100. This was agreed at the experts' meeting and the NOAEL based on haematological effects was also defined as the overall short term NOAEL including 90-day study in the dog. No correction for oral absorption for the AOEL was

considered needed. Worth to note, regarding the ADI, is that the NOAEL in the long term studies was in the same range. Thus, the appointed NOAEL for both ADI and AOEL could be said to be based on an overall assessment. **The ADI and AOEL is 0.035 mg/kg bw/day.**

ARfD

The Rapporteur member state proposed to set the ARfD on the NOAEL of 10 mg/kg bw from the acute neurotoxicity study in the rat applying the safety factor of 100. This was agreed at the experts' meeting. **The ARfD is 0.1 mg/kg bw.**

2.11 DERMAL ABSORPTION

One *in vitro* study on rat and human skin was submitted in the dossier and evaluated in the DAR. However, there were several deficiencies in the test protocol and thus the quality and reliability of the study was questioned by several Member States. Therefore, the notifier submitted new studies, an *in vivo* study as well as *in vitro* studies in rat and human skin, which were evaluated and presented in the Addendum (September 2004, compiled December 2004). The setting of dermal absorption value was discussed at the experts' meeting.

Initially, based on the first *in vitro* study, the Rapporteur member state had proposed to use 0.1% for the concentrate and 25% for the spray dilution pending confirmatory data.

Based on the *in vivo* study dermal penetration values of 47% for the dilution and 0.5% for the concentrate were proposed. The results from the *in vitro* studies showed that the rat penetration was higher than the human and that as a worst case an approximate ratio would be assumed to 2.3. Taking this correction factor into consideration the revised proposal for dermal absorption was 0.1 % for the concentrate and 13% for the dilution.

The experts' meeting agreed to the proposal. It should be noted that it was discussed and concluded that in this case the amount in the skin depot was not considered as bioavailable.

2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Aphox/Pirimor is a wettable granular (WG) containing 500 g pirimicarb/kg for use on wheat.

Operator exposure

According to the intended uses submitted by the notifier the maximum applied dose is 420 g product/ha (210 g pirimicarb/ha) and the minimum volume 200 L. The only considered supported use was tractor mounted field crop sprayer with hydraulic nozzles.

The estimated operator exposure was revised after finalising the DAR since the dermal absorption value was changed. New calculations were presented in the Addendum (September 2004, compiled December 2004) which was discussed at the experts´ meeting. EFSA notes that in table 12 where the estimated operator exposure using the UK POEM are presented, the dermal absorption values are given for trifloxystrobin, however the ones used are actually the correct ones set for pirimicarb.

The estimated operator exposure for Aphox/Primor 50WG is below the AOEL without PPE, according to German model (work rate 20 ha/day). According to calculations with UK POEM, (work rate 50 ha/day) gloves and respiratory protective equipment (RPE) have to be used during mixing and loading (M/L) as well as gloves during application and when handling contaminated surfaces, in order to be below the AOEL (see table below).
Even if the estimations according to the German model are below the AOEL without PPE, it would be justified to include the use of gloves and RPE due to the sensitizing properties of pirimicarb and due to the fact that it is toxic during acute oral and inhalation exposure, see 2.2. This would also be needed if a work rate of higher than 20 ha/day would be reality. If coverall is used, the estimated exposure is <10% of the AOEL according to calculations in the German model.

Estimated exposure presented as % of AOEL (0.035 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	**No PPE**	**With PPE** Only when handling concentrate:	**With PPE* and RPE** When handling concentrate and dilution:
German	47%	47%	37%
UK POEM	397%	394%	57%

* PPE (personal protective equipment): gloves during application and when handling contaminated surfaces
RPE (respiratory protection equipment): filtering facepiece respirator (EN FFP2).

Worker exposure

A German re-entry model18 was used for the calculations of worker exposure. According to the revised dermal absorption value, the estimated worker exposure would be approximately 23% of the AOEL.

Bystander exposure

Estimated exposure to bystanders was made according to an UK model19 for field crop sprayers. Based on the 13% dermal absorption and assuming a body weight of 60 kg the estimated acute exposure of a bystander is approximately 1% of the AOEL.

[18] Hoenicke *et al.*, 1998. Hinweise in der Gebrauchsanleitung zum Schutz von Personen bei Nachfolgearbeiten in mit Pflantzenschutzmitteln behandelten Kulturen. Nachrichtenbl. Deut. Pflantzenschutzd. 50 (10), p 267.
[19] Lloyd and Bell, 1983. Hydraulic nozzles: comparative spray drift study.

3. Residues

Pirimicarb was discussed at the EPCO experts' meeting for residues (EPCO 15) in October 2004.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of [^{14}C]pirimicarb has been studied on four crops, representative of 4 major plant groups: lettuce (leafy vegetables), potatoes (root vegetables), apples (fruits) and wheat (cereals). Studies in lettuce, potatoes and apples are considered as supportive information, but their outcome cannot be considered for fixing a residue definition for the plant groups they are belonging to as it is not possible to assess their appropriateness in the absence of information on the actual or intended use of pirimicarb on those commodities.

In the investigated crops, parent residues were generally higher than 10% of the Total Radioactive Residues (TRR) in the edible fractions of the plants. Carbamate metabolites were also present at lower levels than the parent compound, R34836, R35140 and R34885. In wheat grains, R35140 was not present. Other metabolites resulting from the loss of the carbamate moiety and later from the cleavage of the pyridine ring were also identified but are of no toxicological significance. Among the carbamate metabolites, R34836 showed in all cases the highest absolute amounts, although it should be considered that R35140 and R34885 represent a similar toxicological burden due to their higher acute toxicity.

In theory, all these metabolites should be included in the residue definition. From an analytical point of view, a validated method of analysis was submitted allowing determination of pirimicarb, R34836 and R34885. Because this method covers most of the global toxicological burden of residues generated by the use of pirimicarb, the residue definition for monitoring and risk assessment can be established as the sum of pirimicarb, R34836 and R34885, expressed as pirimicarb. There is no need to include R35140 in the residue definition for risk assessment in the case of the use on wheat.

Supervised residue trials were conducted on wheat in Northern and Southern parts of the EU, in accordance with the representative uses. Data concerning the storage stability of the residues demonstrated their stability under the storage conditions of the trials. The information resulting from these trials is sufficient to predict the exposure of the consumer resulting from the use of pirimicarb in wheat and to proposed MRLs. Residues in wheat grains ranged from < 0.02 mg/kg up to 0.06 mg/kg. Samples where residues were measurable confirmed that the parent molecule is the predominant compound of the residue. In straw the highest residue level found amounted to 1.20 mg/kg.

No data were submitted concerning the effects of industrial and/or household preparation on the nature of residues as the residue level in grains is low and intake calculations result in expected chronic and acute exposures far below the toxicological critical end points.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

A confined rotational crop study was carried out with pirimicarb applied at a single dose representing 7 fold the application rate of the representative use in cereals. Crops of lettuce, radish and millet were planted 29, 61 and 119 days after soil treatment and were harvested at maturity. In lettuce and radish roots planted 29 and 61 days after treatment, residues of pirimicarb and metabolites relevant for the residue definition were present in the range of the limit of determination of the method of analysis. Under practical conditions, at normal application rate and taking into account the level of interception of the product applied by the plants, no measurable residues of pirimicarb and its metabolites should be present on succeeding and rotational crops. Therefore, no cropping restriction nor MRL are proposed to be fixed for succeeding and rotational crops.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Metabolism studies were conducted with orally administered [^{14}C]pirimicarb in goats and hens. The dose administered to animals was largely in excess of the expected practical level of exposure of livestock (about 20, 60 and 200 fold for beef cattle, dairy cattle and poultry respectively). In these extreme conditions, no parent or other carbamate compounds were found in edible tissues. Only small amounts (lower than 10 mg/kg) of non-carbamate residues were present. Therefore a default residue definition consisting of pirimicarb only is proposed. However the monitoring of animal products is not necessary in terms of consumer safety.

Based on the outcome of the metabolism studies, no feeding studies in livestock are required.

3.3. CONSUMER RISK ASSESSMENT

A chronic dietary risk assessment has been carried out according to the WHO Theoretical Maximum Daily Intake (TMDI) calculation model using the WHO European typical diet and the MRL proposed for wheat. This resulted in a total intake of residues representing 2% of the ADI.

A short term exposure risk assessment was carried out using the WHO methodology and the large portion consumption data of United Kingdom for adults and $1^{1/2}$ to $4^{1/2}$ year old toddlers. The National Estimated Short Term Intakes resulting from the consumption of wheat products were calculated to be below 1 % of the ARfD for both adults and toddlers. The exposure of extreme British consumers, including infants and children, was calculated to be 1 to 2% of the ADI, taking into account the median value of the residue levels in wheat.

In conclusion, no risk was identified neither from the chronic nor from the acute exposures to residues resulting from the use of pirimicarb according to the representative use on wheat.

3.4. PROPOSED MRLS

Based on the available data base, a MRL of 0.1 mg/kg for wheat can be proposed to cover the representative uses supported by the applicant. MRL's for animal commodities are not needed.

4. Environmental fate and behaviour

4.1. FATE AND BEHAVIOUR IN SOIL

Open points and new data provided for pirimicarb were discussed in Experts Meeting on Fate and Behaviour in the Environment (EPCO 12, September 2004).

4.1.1. ROUTE OF DEGRADATION IN SOIL

Pirimicarb metabolism in soil under dark aerobic conditions at 20 °C was investigated in a study with three different soils. The three soils were very similar with respect to pH (6.4-7.1) and covered a range of clay contents (12 % - 20 %) and organic matters content (1.0 % - 4.9 %). The studies were run for up to 372 d but it was considered that microbial activity was maintained thought the test period.

Under aerobic conditions, initial transformations of pirimicarb in soil involve either the dimethyl amino group producing the two metabolites **R34885** (maximum 12.4 % AR after 14 d) and **R34836** (maximum 9.3 % AR after 140 d), the carbamate moiety producing the metabolite **R31805** (maximum aprox. 26.5 % AR after 168 d) or both moieties yielding the metabolite **R34865** (maximum 31.2 % AR after 372 d). Metabolite R34836 does not reaches the 10 % AR in soil at any time point but was considered relevant due to the fact that still contains the intact carbamate toxophore. Mineralization after 103 d was low (maximum 3 % AR) and unextractable residues accounted for a maximum of 14.9 % AR after 84 d.

In the same study degradation under dark anaerobic conditions at 20 °C was investigated in one sandy loam soil. Under these conditions only metabolite R31805 was found at amounts above 10 % AR (maximum 28.5 % AR after 372 d). No new metabolites with respect to aerobic route were identified.

Photolysis in soil may contribute to the environmental degradation of pirimicarb. Metabolite R34836 was the only photoproduct found at amounts above 10 % AR.

Dissipation of pirimicarb under field conditions was investigated in two field studies. One of the studies was performed in California USA (one location two plots) and the other in Germany EU (four locations).In the California field study the metabolite **R35140** containing the carbamate moiety was identified at average levels of 1.98 % of applied amount. Due to the fact that it contains the carbamate moiety it is considered as a relevant metabolite for soil compartment.

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

Degradation rate of pirimicarb under aerobic and anaerobic conditions was investigated in the same study used to establish the route of degradation in soil. Fitting to first order kinetics was poor for two of the three soils and therefore fitting to FOMC was also provided. Pirimicarb is medium to high persistent in soil ($DT_{50\ 20°C\ FMOC}$ = 29 – 143 d).

Evaluation Meeting (May 2004) expressed concerns on the narrow range of soil pHs tested. One MS informed that data available to their authorities contained studies performed at lower pH and that

longer half-lives were observed. A data requirement was set for these studies, the concerned MS agreed to provide the references of the related studies to the RMS. The references were provided to the RMS during the experts' meeting. After the meeting, RMS received an evaluation document from the concerned MS summarizing the results of three laboratory degradation studies performed in the 1970s. RMS discusses this summary in an Addendum 4 to the DAR (December 2004). Since the original reports are still not available for evaluation these results are not considered in this conclusion. Therefore, the confirmatory data requirement is maintained for these studies. However, it is the opinion of the RMS that, according the summary available to them, the trend for longer DT_{50} at lower pH is not fully consistent and that no evidence of pH effects are observed in the aqueous hydrolysis study (pirimicarb stable at pH 5-9). Additionally, EFSA notes that seven of the nine values reported are within the range of half-lives obtained in the study available in the dossier. Nevertheless, degradation in an additional soil would be necessary to fulfil data requirement as given in directive 91/414/EEC Annex II 7.1.1.2.1. RMS proposed in the DAR that since enough field studies are available there are sufficient data for EU risk assessment. However, EPCO meeting agreed that field studies will only represent situations were the product is fully exposed to light (bare soil application) and that representative uses proposed are not fully represented by them (cropped soil). Furthermore, the notifier failed to provide validation data for the analytical method employed in field soil studies at LOQ = 0.01 mg / kg. Experts meeting considered that field studies may qualitatively indicate a shorter persistence in field under bare soil conditions but no reliable DT_{50} may be obtained from them. Therefore, it is the EFSA opinion that further laboratory degradation data with at least an additional soil under aerobic conditions is still needed. If the studies to be submitted with respect to the data requirement set by Evaluation Meeting (see above) are finally not found acceptable to cover this data gap new data may need to be generated and provided.

There are separated degradation studies to investigate the degradation in three different soils under dark aerobic conditions at 20 °C for the metabolites R34836, R31805 and R34865. Metabolite R34836 is low to medium persistent ($DT_{50\ 20°C}$ = 7 d – 90 d), R31805 is moderately persistent ($DT_{50\ 20°C}$ = 33 d – 38 d) and R34865 is moderate to medium persistent ($DT_{50\ 20°C}$ = 37 d – 78 d). For metabolite R34885, degradation parameters were estimated with a multi-compartmental model using data obtained in the laboratory study performed with the parent pirimicarb. This metabolite appears to be moderately persistent in soil ($DT_{50\ 20°C}$ = 14 d – 31 d).

Photolysis in soil may contribute to pirimicarb dissipation. Degradation did not follow first order kinetics and RMS calculated DT50 according sqr 1.5 order.

In the field studies performed in California (USA) and Germany (EU) first order half-lives between 5 d and 46 d were calculated. However, for two soils R^2 was between 0.7 and 0.85 and sqr 1.5 order was calculated and reported in the DAR. Initially, RMS used field half life to calculate PEC soil. This was not accepted by the experts meetings because field studies were performed in bare soil and representative uses imply application to fully developed crops. It is considered that for pirimicarb photolysis may have an important role on the degradation. The contribution of this degradation route may have been overestimated in the bare soil studies with respect to the lower irradiation in the cropped field. Therefore, worst case laboratory DT_{50} = 150 d was agreed for PEC soil calculations.

Consequently new PEC soil calculations have been presented by the RMS in the addendum to the DAR (December 2004).

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

Batch adsorption/desorption studies are available for pirimicarb and metabolites R34836, R34885, R31805 and R34865. The results for these studies indicate that pirimicarb is low to high mobile (K_{foc} = 45 – 730 mL / g), R34836 could be classified as slightly to very high mobile (K_{foc} = 33.6 – 4320 mL / g), R34885 low to high mobile (K_{foc} = 57.2 – 867 mL / g), R31805 immobile to high mobile (K_{foc} = 130 – 80000 mL / g) and R34865 immobile to medium mobile (K_{foc} = 179 – 9650 mL / g). Mobility of all these compounds seem to be very dependent on the soil properties but not consistent trend with respect to pH of other soil properties was identified by the RMS except for metabolite R31805 that appears to present stronger adsorption in more acidic soils. However, experts meeting considered that a dependence of the K_{foc} values on the soil clay content could be deduced and therefore ask RMS to include this information in the list of end points to be considered by MS in their assessments. Column leaching studies, field leaching studies and lysimeters are not available.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

In sterile buffer solutions at 25 °C, pyrimicarb was found to be stable to hydrolysis at environmental relevant pH 5 to 9.

Three separated studies investigated the photochemical degradation of pirimicarb in water. These studies indicate that photochemical half-life of pirimicarb in water under mid-European conditions is relatively rapid ($DT_{50\ (30\ cm\ depth)}$ = 12 h to 12 d). Three major photochemical metabolites were identified: R34885 (maximum at pH 5: 17.9 % after eq. 30 h summer 30°N), R31805 (maximum at pH 5: 27.8 % after eq. 30 h summer 30°N) and **R16210**[20] (maximum at pH 7: 26.9 % after eq. 30 h summer 30°N).

No ready biodegradability test is available; experts meeting considered pirimicarb to be not ready biodegradable based on water sediment study.

A study with two water sediment systems is available. Pirimicarb partitions slowly from the water to the sediment ($DT_{50\ whole\ system}$ = 156 – 183 d; $DT_{50\ water}$ = 36 – 55 d). Degradation of pirimicarb in the sediment is very limited and no reliable half life was calculated. Up to 13 transformation products were separated but none of them above 10 % AR. Three of them were identified as R34885, R34836 and R31805 (below 4 % AR each). Pirimicarb remained the major component in both the water and sediment compartments. Unextractable radioactivity in sediment increased during the 100 d that lasted the experiments up to 13 % and 10 % AR. Mineralization was very low with a maximum of 1.5 % of CO_2 formed after 100 d.

Surface water risk assessment presented in the DAR is based on spray drift route of entry to surface water and considered photolysis in water (DT_{50} < 1d) as the main route of dissipation.

[20] R16210: 1,1-dimethylguanidine, dimethylguanidine

The experts meeting discussed the environmental relevance of aquatic photolysis. Whereas acknowledging that photolysis may play an important role to the dissipation of pirimicarb in certain environmental conditions, risk assessment based on a non photolysis situation must be considered for EU evaluation in agreement with previous ECCO and EPCO meeting decisions. Therefore, PECsw were recalculated based on the longest first order half life (DT_{50} = 55d) for the water phase of the dark water/sediment system (Addendum 4, December 2004).

Other routes of potential surface water contamination as drainage and run off were not considered in the DAR based on the presumed low persistence in soil derived from field studies results. As summarized in the soil section, for the representative uses proposed results of field studies are not directly applicable and persistence in soil of pirimicarb was consequently revised based on a laboratory DT_{50} = 150 d. Therefore, potential surface water contamination through run off and drainage may not be precluded based on the available data. Consequently, it is the EFSA opinion that surface water risk assessment may not be considered complete without addressing these other routes of potential ground water contamination. Experts meeting also agreed that potential surface water contamination thought volatilization and deposition may need to be assessed for pirimicarb.

Potential for accumulation of pirimicarb into the sediment was identified by the experts meeting. Since no reliable half life in the sediment may be obtained from the available water sediment study, a reasonable worst case estimation was done by using DT_{50} = 335 d from the anaerobic soil degradation study. This value was used to calculate an accumulated PEC_{sed} = 29 µg / kg (Addendum 4, December 2004). However, as for the PECsw calculations this value only incorporates potential loadings through spray drift.

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

The potential leaching of pirimicarb and its metabolites R34836, R34885, R31805, R34865 to ground water was simulated with FOCUS PELMO 3.3.2 for the nine FOCUSgw scenarios. The geometric mean of the laboratory first order DT_{50}s and mean K_{foc} and 1/n were used as input parameter. For pirimicarb this means that a geometric mean DT_{50} = 100.2 d was used including one value with a fitting $r^2 < 0.7$. Since only three soils were tested and of them only two fitted to first order with a $r^2 > 0.7$, worst case $DT_{50\ 20°C\ 10\ k\ Pa}$ = 150 d should have been use for modelling purposes.[21] However, the resulting concentration for all the nine scenarios were below 0.001 µg / L and it is not expected that the trigger 0.1 µg / L would be exceeded using a half life a 50 % longer. MS may also need to consider the K_{foc} dependence on soil clay content. Soil metabolite R35140 identified in some field studies has not been assessed for potential ground water contamination. Taking into account that the average amount found in these studies for this metabolite was of 2 % of applied dose and the structural similarities with other metabolites assessed, EFSA is of the opinion that it is very unlikely that the trigger of 0.1 µg / L would be exceeded by this metabolite. However, it needs to be properly addressed due the fact that it is more acutely toxic than the parent pirimicarb.

[21] Generic guidance for FOCUS groundwater scenarios. V.1.1 April 2002.

4.3. FATE AND BEHAVIOUR IN AIR

Concentration of pirimicarb in the air compartment and transport through it is not expected to be significant. Although some potential volatilization from leaf surface was observed, calculation according Atkinson model indicate that it will degrade in the atmosphere with a estimated half life of less than 1 h. Experts meeting agreed that potential surface water contamination thought short range volatilization and deposition may need to be assessed for pirimicarb.

5. Ecotoxicology

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk to birds and mammals was calculated using residue data outlined in EPPO (1992).

The risk was calculated for an insectivorous bird as the representative use is in cereals at a late stage when it is considered unlikely that grazing of the crop will occur. In the first tier risk assessment the Annex VI trigger value is breached at an acute time scale (TER=4.77) indicating a high acute risk to birds. The TER values for the short and long term risk (TER-values are 296 and 9.85 respectively) are above the Annex VI trigger values indicating a low short and long term risk to birds.
A refinement of the acute risk is available in the DAR. This refinement is based on the time quotient approach and the observation that no mortalities occurred in the long term toxicity study at a dose above the acute estimated theoretical exposure (ETE). This was discussed at the EPCO experts' meeting on ecotoxicology (EPCO 13) and the meeting decided to seek an opinion of the PPR panel. The question was forwarded to the Panel by EFSA. The PPR Panel assessed the risk to birds feeding on insects in the field after treatment of cereals with pirimicarb. The acute TER based on the LD_{50} from an acute gavage study was 4.77, whereas a short-term TER based on the LD_{50} estimated from a 5-day dietary study was 92.5. However, neither the acute gavage study nor the 5-day dietary study closely represents the pattern of exposure expected in the field. Therefore, the PPR Panel carried out a refined assessment taking account of expected feeding rates of wild birds, the toxicokinetic and toxicodynamic characteristics of pirimicarb, and the reduction of exposure due to food avoidance. Based on the results of this assessment, the PPR Panel is of the opinion that even at the upper limit of credible exposures, birds feeding on insects in the field are unlikely to achieve a lethal dose of pirimicarb.[22]

Furthermore the risk to insectivorous mammals was calculated. As for birds the scenario for herbivorous mammals is not considered relevant as the representative use is in cereals at a late stage when it is considered unlikely that grazing of the crop will occur. The TER values for the acute and long term risk (TER-values are 346 and 1323 respectively) are above the Annex VI trigger values indicating a low acute and long term risk to mammals.

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

As the risk to birds and mammals was calculated according to EPPO (1992), a similar risk assessment was made available by EFSA based on the "Guidance Document on Risk Assessment for Birds and Mammals under Council Directive 91/414/EEC" (Sanco/4145/2000 of 25 September 2002). According to this assessment (see addendum by EFSA) the risk to mammals can be regarded as low as the calculated acute and long term TER values (TER-values are 76.7 and 121.2 respectively) are above the respective Annex VI trigger values for the representative uses evaluated. Also the short term risk to birds (TER = 62.2) can be regarded as low as the calculated TER value is above the respective Annex VI trigger values for the representative uses evaluated. But the Annex VI trigger value for the acute and long term risk (TER-values are 1.84 and 1.91 respectively) is breached indicating a high acute and long term risk to birds in the first tier risk assessment. Therefore EFSA proposes a data requirement for the notifier to submit a refinement of the long term risk to birds if the risk is assessed according to the latest guidance document (SANCO/4145/2000). For the acute risk to birds see opinion of the PPR Panel discussed above.

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

5.2. RISK TO AQUATIC ORGANISMS

Daphnia magna is the most sensitive aquatic organism on an acute and chronic time-scale when tested with pirimicarb. The lead formulation was only tested on *Daphnia magna* as this species is more than one order of magnitude more sensitive to pirimicarb than the other aquatic species tested. Based on this study it was observed that the formulation showed a similar toxicity to *Daphnia magna* as the a.s.

The resulting acute TER-value for *Daphnia magna* at 1 m from a field (5.33) is below and hence breaches the Annex VI trigger value of 100 so the acute risk to aquatic organisms should be considered as high.

Several other aquatic invertebrates were tested (several Crustacea and Insecta species, 2 Gastropoda species and one Hirudinea, Turbellaria and Protozoa). All these species were less sensitive to pirimicarb than *Daphnia magna*. Furthermore one additional Cladocera species (*Daphnia pulex*) was tested which showed similar sensitivity to pirimicarb as *D. magna*. As it appeared from these studies that cladocerans (represented by *D. magna* and *D. pulex*) are at least one order of magnitude more sensitive to pirimicarb than other freshwater fauna it was considered appropriate by the RMS to lower the Annex VI trigger value from 100 to 10 as discussed in the Guidance Document on Aquatic Ecotoxicology (SANCO/3268/2001 rev. 4 (final) dated 17 October 2002). This was agreed upon by the EPCO 13 experts' meeting on ecotoxicology.

But as the TER for *D. magna* is still below this trigger, the RMS proposed to refine the risk further based on studies which included sediment. This was also discussed by the EPCO 13 experts' meeting. The meeting decided to await the opinion of PPR Panel on the question on Dimoxystrobin as this question also includes a study in the presence of sediment. Furthermore, the meeting asked the RMS to make TER calculations available which include bufferzones and to take into account the revised

PECsw values by the EPCO 12 experts' meeting on fate and behaviour. These calculations are made available by the RMS in the addendum 4 of December 2004. EFSA agrees with the calculations presented in the addendum. Based on these calculations the acute risk to aquatic organisms can be considered as low if a bufferzone of 5 metres is taken into account based on the standard acute toxicity study to *D. magna* without the presence of sediment. Any further refinements of the risk to aquatic organisms based on studies in the presence of sediment should be performed in accordance with the opinion of the Scientific Panel (PPR) on dimoxystrobin[23].

The standard long term TER-value for *D. magna* at 1 m from a field (0.28) is below and hence breaches the Annex VI trigger value of 10 so the long term risk to aquatic organisms should be considered as high. To refine this risk the RMS proposes to use a study in the presence of sediment. This was discussed at the EPCO 13 experts' meeting on ecotoxicology and it was decided to await the opinion of PPR Panel on the question on Dimoxystrobin as discussed above for the acute risk. In addendum 4 also the long term risk was recalculated. As asked by the experts' meeting the RMS calculated a TER value taking into account a bufferzone of 5 m for the standard chronic study without the presence of sediment. As this bufferzone is not sufficient to meet the triggervalue EFSA calculated that a bufferzone of 40 meter (TER=11.2, see addendum by EFSA) will be necessary to meet the Annex VI trigger value if the risk assessment is based on the standard chronic study with *D. magna*. Any further refinements of the risk to aquatic organisms based on studies in the presence of sediment should be performed in accordance with the opinion of the Scientific Panel on dimoxystrobin.[1]

Pirimicarb can be found in concentrations above 10% of the AR in the sediment. Therefore the risk to sediment dwelling organisms needs to be addressed. Two acute toxicity studies with *Chironomus riparius* are available. Based on these studies it can be concluded that pirimicarb is more than one order of magnitude less acutely toxic to sediment dwelling organisms than to *Daphnia magna*. The range of aquatic invertebrate species tested give an indication that pirimicarb is rather selective against daphnids. Therefore it was considered that the risk to sediment dwelling organisms will be covered by the assessment of the risk to *Daphnia magna*. This was agreed by the EPCO 13 experts' meeting.

Furthermore the metabolites R35140, R34836, R34885, R31805, R34865 and R16210 were tested on *Daphnia magna*. R34865 was additionally tested on rainbow trout and R34865 and R31805 were additionally tested on algae. As for the parent *Daphnia magna* was the most sensitive species tested with the metabolites. R31805, R34865 and R16210 are more than one order of magnitude less toxic to *D. magna* than the parent. R35140, R34836 and R34885 show a similar toxicity to *D. magna* as the parent. The risk from the metabolites is considered to be covered by the risk assessment for the parent compound.

[23] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR) on a request from EFSA related to the evaluation of dimoxystrobin. *The EFSA Journal* (2005) 178, 1-45.

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

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

5.3. RISK TO BEES

Acute contact and oral toxicity studies both with pirimicarb and the lead formulation are available. The resulting HQ values for the lead formulation do not breach the appropriate Annex VI trigger value indicating a low risk to bees from the lead formulation.

The oral HQ value (52.5) for the a.s. breaches the Annex VI trigger value indicating a high risk to bees from the a.s. via the oral route while the risk to bees from the a.s. via the contact route (HQ = 3.95) can be considered as low. Field studies to address this risk which cover the representative uses under evaluation are available. The risk to bees was discussed at the EPCO 13 experts' meeting and the meeting agreed that the risk to bees is addressed with the data available and hence no further data or risk mitigation measures were considered necessary.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Since insecticidal effects were expected in first tier studies, the available studies were performed according to more realistic Tier II and extended laboratory testing procedures.

Extended laboratory studies with *Typhlodromus pyri*, *Aphidius rhopalosiphi*, *Chrysoperla carnea*, *Episyrphus balteatus*, *Pardosa* spp. and *Pterostichus melanarius* are available. Furthermore a field study carried out in a field of spring barley in Denmark is available as well as a review of additional laboratory and field data from various sources.

Episyrphus balteatus is the most sensitive species tested with an LR_{50} of 14.6 g a.s./ha in an extended laboratory study. In the field study in spring barley no direct 'biological significant' effects were observed on the non-target arthropod studied after 1 application of 125 g a.s./ha. The only effective sampling method in this study was by using pitfall traps and this method would not have been able to identify adverse effects on the populations of many foliage dwelling species including Syrphidae. In the review of additional field data, effects on Syrphidae were observed at dose rates which cover the application rates of the representative uses.

The risk to non-target arthropods was discussed at the EPCO 13 experts' meeting. The meeting decided that based on the available residue decline data (DT_{50} = 1.2 d) on foliage, population recovery/recolonisation would be possible within one year. Therefore the meeting also discussed the off-field risk. The meeting agreed that the risk to non-target arthropods is addressed when comparing the maximum off-field field rate at 1 m from the field for the representative uses evaluated (6.4 g a.s./ha) to the LR_{50} of 14.6 g a.s./ha (extended lab) for the most sensitive species *Episyrphus balteatus*.

5.5. RISK TO EARTHWORMS

Studies on the acute toxicity to earthworms from a 50 % WG formulation (YF 7321 A) and the metabolites R31805 and R34865 are available. The endpoints were not corrected as the logPow is

below 2. The TER-values resulting from the endpoints derived from these studies do not breach the Annex VI trigger value (TER>178) indicating a low acute risk to earthworms for the representative uses.

No studies on the effects on reproduction are available but a field study was submitted. In this field study pirimicarb was applied at concentrations exceeding the application rate of the representative uses for up to 5 consecutive years. In this study no adverse effects on earthworms were observed.

No studies with the metabolites R34885, R35140 and R34836 are available. No studies are considered necessary as it is assumed that these metabolites were present during the 5-year field study and hence the risk from these metabolites is considered to be covered by this field study.

Based on the available data the risk to earthworms from pirimicarb and the metabolites R31805, R35140, R34865, R34885 and R34836 can be regarded as low for the representative uses evaluated.

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

No studies on the effects of pirimicarb on other soil non-target macro-organisms were considered necessary as the risk to earthworms and soil micro-organisms is considered to be low. Furthermore the effects on the indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri* were less than 50% at the doses in-field expected from the representative uses evaluated. This is supported by a field study where only indirect effects were seen on Collembola at 125 g a.s./ha and the report of no significant differences in the number or diversity of micro-arthropods found at 500 g a.s./ha in the earthworm field study. Therefore the risk to soil non-target macro-organisms from pirimicarb is considered low for the representative uses evaluated.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of a 50 % WG formulation (YF 7321 A) and the metabolites R31805 and R34865 were tested on soil microbial respiration and nitrogen transformation. No deviations of more than 25 % after 14 days were observed (i.e. no breaching of the Annex VI trigger value) and hence the risk to soil non-target micro-organisms from pirimicarb and the metabolites R31805 and R34865 is considered to be low.

No studies with the metabolites R35140, R34885 and R34836 are considered necessary by the RMS as they are considered to be minor and no effects were seen on the parent and the tested metabolites R31805 and R34865. It is noted by EFSA that the metabolites R35140, R34885 and R34836 are considered major and/or relevant metabolites by the section on Fate and Behaviour. R35140 and R34885 still contain the carbamate moiety. Therefore, EFSA proposes that a study or at least a solid argumentation regarding the effects of the metabolites R35140, R34885 and R34836 on soil non-target micro-organisms should be made available. The need for these data was not discussed at an EPCO experts' meeting.

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

Studies on the effects of the lead formulation on non-target terrestrial plants are available. Effects were less than 20% at a dose rate exceeding the highest representative use rate. Therefore the risk to non-target plants is considered to be low.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The 6 hour IC_{50} for pirimicarb to *Pseudomonas putida* exceeds 2700 mg/L. Based on this study the risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: pirimicarb, R34885[24], R34836[25], R31805[26], R34865[27], R35140[28].

Definitions for monitoring: pirimicarb, R34885 (pending on assessment on effects on soil non-target micro-organisms), R34836 (pending on assessment on effects on soil non-target micro-organisms), R35140 (pending on assessment on effects on soil non-target micro-organisms).

Water

Ground water

Definitions for risk assessment: pirimicarb, R34885, R34836, R31805, R34865, R35140.

Definitions for monitoring: pirimicarb, R35140 (pending on assessment on potential ground water contamination).

Surface water

Definitions for risk assessment: pirimicarb (water and sediment), R34885, R31805, R16210[29] (photolysis metabolites).

Definitions for monitoring: pirimicarb

Air

Definitions for risk assessment: pirimicarb

Definitions for monitoring: pirimicarb

[24] R34885: 5,6-dimethyl-2-(methylformamido)pyrimidin-4-yl dimethylcarbamate
[25] R34836 : 5,6-dimethyl-2-(methylamino)pyrimidin-4-yl dimethylcarbamate
[26] R31805: 2-dimethylamino-5,6-dimethylpyrimidin-4-ol
[27] R34865: 5,6-dimethyl-2-(methylamino)pyrimidin-4-ol
[28] R35140: 2-amino-5,6-dimethylpyrimidin-4-yl dimethylcarbamate
[29] R16210: 1,1-dimethylguanidine

Food of plant origin
Definitions for risk assessment: sum of pirimicarb, R34836 and R34885, expressed as pirimicarb
Definitions for monitoring: sum of pirimicarb, R34836 and R34885, expressed as pirimicarb

Food of animal origin
Definitions for risk assessment: pirimicarb
Definitions for monitoring: pirimicarb

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
pirimicarb	Medium to high persistent ($DT_{50\ 20°C\ FMOC}$ = 29 – 143 d)	See 5.5, 5.6 and 5.7
R34885 (contains the carbamate moiety)	Moderately persistent in soil ($DT_{50\ 20°C}$ = 14 d – 31 d)	The risk to earthworms can be regarded as low. No study with micro-organisms is available.
R34836 (contains the carbamate moiety)	Low to medium persistent ($DT_{50\ 20°C}$ = 7 d – 90 d)	The risk to earthworms can be regarded as low. No study with micro-organisms is available.
R31805	Moderately persistent ($DT_{50\ 20°C}$ = 33 d – 38 d)	The risk to earthworms and soil micro-organisms can be regarded as low.
R34865	Moderate to medium persistent ($DT_{50\ 20°C}$ = 37 d – 78 d)	The risk to earthworms and soil micro-organisms can be regarded as low.
R35140 (contains the carbamate moiety)	Sporadically found in field studies at a maximum average amount of 2% of applied dose	The risk to earthworms can be regarded as low. No study with micro-organisms is available.

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
pirimicarb	low to high mobile (K_{foc} = 76 – 730 mL / g)	FOCUS PELMO: 0.1 µg/L trigger not exceeded.	Yes	Yes	See 5.2

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
R34885 (contains the carbamate moiety)	low to high mobile (K_{foc} = 57.2 – 867 mL / g)	FOCUS PELMO: 0.1 µg/L trigger not exceeded	No assessment required. No data available.	Toxicologically relevant. LD_{50} 50-100 mg/kg bw/day No study on genotoxicity available	No assessment required. Data available (*Daphnia magna*). Similar toxicity than parent.
R34836 (contains the carbamate moiety)	slightly to very high mobile (K_{foc} = 33.6 – 4320 mL / g)	FOCUS PELMO: 0.1 µg/L trigger not exceeded	No assessment required. No data available.	Toxicologically relevant LD_{50} 200-400 mg/kg bw/day No study on genotoxicity available	No assessment required. Data available (*Daphnia magna*). Similar toxicity than parent.
R31805	immobile to high mobile (K_{foc} = 130 – 80000 mL / g)	FOCUS PELMO: 0.1 µg/L trigger not exceeded	No assessment required. No data available.	Not toxicologically relevant LD_{50} 800-1600 mg/kg bw/day Genotoxicity: mutagenic *in vitro*, but negative *in vivo*	No assessment required. Data available (*Daphnia magna*, algae). Less toxic than the parent.
R34865	immobile to medium mobile (K_{foc} = 179 – 9650 mL / g)	FOCUS PELMO: 0.1 µg/L trigger not exceeded	No assessment required. No data available.	Not toxicologically relevant LD_{50} > 2000 mg/kg bw/day Genotoxicity: mutagenic *in vitro*, but negative *in vivo*	No assessment required. Data available (*Daphnia magna*, fish, algae). Less toxic than the parent.
R35140 (contains the carbamate moiety)	Not assessed	Not assessed	No data available.	Toxicologically relevant. LD50 79 mg/kg bw/day No study on genotoxicity available	Data available (Daphnia magna). Similar toxicity than parent.

Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Pirimicarb (water and sed)	See 5.2
R34885 (photolysis metabolite, contains the carbamate moiety)	No assessment required. Data available (*Daphnia magna*). Similar toxicity than parent.
R31805 (photolysis metabolite)	No assessment required. Data available (*Daphnia magna*, algae). Less toxic than the parent.
R16210 (photolysis metabolite)	No assessment required. Data available (*Daphnia magna*, algae). Less toxic than the parent.

Air

Compound (name and/or code)	**Toxicology**
Pirimicarb	Toxic during acute exposure (T; R25, proposed), no study on repeated exposure available, see 2.2.

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

- Clarification with respect to the proposed maximum levels for impurities in the technical material (data requirement identified in the evaluation meeting and confirmed by experts' meeting, September 2004; date of submission unknown; refer to chapter 1)
- A study for the determination of the boiling point/temperature of decomposition (announced by the notifier for end August 2004 refer to chapter 1)
  In the meantime RMS has received a study but has not evaluated it.
- Notifier should address the applicability of the EEC method A 8 for the determination of the *n*-octanol/water partition coefficient (open point identified in the evaluation meeting and changed into a data requirement by experts' meeting, September 2004; date of submission unknown; refer to chapter 1)
- An ILV for the enforcement method for the determination of residue in food of animal origin (announced by the notifier for mid 2005; refer to chapter 1).
  Due to the fact that in the meantime it was proposed that MRLs are not needed (contrary to what is stated in the DAR), this requirement is redundant.
- Depending on the final residue definitions for soil and ground water analytical methods for the determination of metabolites R34885 (soil) and R35140 (soil/ ground water) could be necessary (refer to chapter 1)
- Since degradation has only been investigated in three soils (instead of four) under aerobic conditions with a very narrow range of pH s and available field studies are not applicable to the representative uses, data requirement on transformation in soil as set in directive 91/414/EEC Annex II 7.1.1.2.1 may not be considered fulfilled. Notifier to submit the following pirimicarb degradation studies in soil already available to one MS:
  - Laboratory studies of the degradation of single applications of the pesticide in soil, in the absence of plants. Unpublished report of ICI provided by ICI, report no. AR 2555 A, 06-01-1975.
  - Pesticide degradation in soil. Unpublished report of ICI provided by ICI, report no. TMJ 1076A (R), 18-12-1974.
  - Fate in soil. Unpublished report of ICI provided by ICI, report no. TMJ 788 A, August 1972.
    In case these studies are finally not found acceptable in the context of directive 91/414/EEC data requirements, at least a laboratory degradation study in an additional aerobic soil should be provided (relevant for all the representative uses evaluated, no submission date yet proposed by the notifier; refer to point 4.1.2)
- Surface water risk assessment may not be considered complete without addressing drainage and run off routes of potential surface water contamination. (As summarized in the soil section, persistence in soil of pirimicarb was revised during the peer review based on a laboratory DT_{50} = 150 d. and, therefore, potential surface water contamination through run off and drainage may not be precluded based on the available data) (relevant for all the representative uses evaluated, no submission date yet proposed by the notifier; refer to point 4.2.1).

- Soil metabolite R35140 needs to be addressed for potential ground water contamination (relevant for all the representative uses evaluated, no submission date yet proposed by the notifier; refer to point 4.2.2).
- Notifier to submit a refinement of the long term risk to birds (proposed by EFSA) (relevant for all representative uses evaluated if the risk is assessed according to the latest guidance document (SANCO/4145/2000), no submission date proposed by the notifier; refer to point 5.1)
- A study or at least a solid argumentation on the effects of the metabolites R35140, R34885 and R34836 on soil non-target micro-organisms. This data requirement is proposed by EFSA and has not been discussed in an EPCO experts' meeting (relevant for all representative uses evaluated; no submission date yet proposed by the notifier; refer to point 5.7)
- It is noted by EFSA that throughout the section on ecotoxicology a formulation YF 7321 A was tested which differs from the lead formulation. Therefore, the composition should be made available to the RMS in order to assess the comparability of YF 7321 A to the lead formulation (relevant for all representative uses evaluated; no submission date yet proposed by the notifier; refer to point 5).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide as proposed by the notifier which comprises broadcast spraying to control aphids in wheat at application rate up 0.21 kg pirimicarb per hectare. Pirimicarb can be used only as insecticide. The representative formulated product for the evaluation was "Pirimor" ("YF7904B"), a water dispersible granule (WG), registered under different trade names in Europe.

Adequate methods are available to monitor all compounds given in the respective finalised residue definition. Only single methods for determine 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.

Pirimicarb is rapidly and nearly completely absorbed. There were numerous of metabolites evident. The toxicity during oral and inhalatory exposure is high. However, the toxicity via dermal route was low. It is not a skin or an eye irritant but is a skin sensitizer. **Proposal for classification T; R23/25 Toxic by inhalation and if swallowed" and R43 "May cause sensitization by skin contact".** Main effects observed during short term exposure were reduction in cholinesterase activity and haematological effects; the relevant oral NOAEL is 3.5 mg/kg bw/day from the 1-year dog. Due to the consistent effects on haematological parameters at relatively low dose levels throughout the

studies **the proposal for classification is R48/22 "Danger of serious damage to health by prolonged oral exposure"**

There is no genotoxic potential for pirimicarb. However, in the mouse there were indications of a possible increase of pulmonary tumours which were outside the upper historical control range (dose level 93.7 and 130.3 mg/kg bw/day for males and females, respectively). The relevance of lung tumours for humans was questioned. The occurrence of tumours in the used strain of mouse is very rare. The NOAEL is 3.7 and 4.7 in males and females, respectively. The experts´ meeting could not come to an agreement whether this was required or not. **Therefore, a question mark is added to the risk phrase and Xn; R40? is proposed "Limited evidence of a carcinogenic effect" and the final decision is to be made by ECB.**

There were no direct effects on reproductive performance or fertility observed, the parental NOAEL was 21.7 mg/kg bw/day and the NOAEL for reproduction was 81.8 mg/kg bw/day. Pirimicarb did not induce teratogenic or foetotoxic effects at non-maternally toxic doses. The NOAEL for maternal and foetal/developmental effects is 10 mg/kg bw/day from the rabbit study.

No sign of neurotoxicity was observed during short term exposure.

The LD_{50} values for metabolites R35140, R34836 and R34855 are in the same range as for pirimicarb.

The ADI and AOEL is 0.035 mg/kg bw/day based on the NOAEL of 3.5 mg/kg bw/day from the 1-year dog study which is also considered as an overall NOAEL (both short tem and long term). The safety factor of 100 is used. **The ARfD is 0.1 mg/kg bw** based on the NOAEL of 10 mg/kg bw from the acute neurotoxicity study in the rat applying the safety factor of 100.

The dermal absorption value set to 0.1 % for the concentrate and 13% for the dilution. The estimated operator exposure according to the German model is below the AOEL without PPE. According to the UK-POEM gloves and respiratory personal equipment (RPE) is needed during mixing and loading and coveralls and gloves when handling contaminated surfaces. Thus, it would be appropriate to include the use of gloves and RPE due to the sensitizing properties of pirimicarb and due to the fact that it is toxic during acute oral and inhalation exposure.

The metabolism of pirimicarb has been studied on wheat and supportive information was provided for 3 other crops. The residues of concern in wheat were found to be pirimicarb itself and 2 carbamate metabolites with similar level of toxicity, R34836 and R34885. In other crops, another metabolite, R35140 was also present. For the use on grain, the proposed residue definition (sum of pirimicarb, RR34836 and R34885 expressed as pirimicarb) for monitoring is efficient to protect adequately the safety of the consumers.

Supervised residue trials conducted on wheat in Northern and Southern Europe suggest an MRL of 0.1 mg/kg for wheat grains to be fixed.

No concern was identified for rotational and succeeding crops.

The metabolism of pirimicarb in ruminant and poultry is extensive and the use of pirimicarb in wheat does not lead to the presence of the active substance or its carbamate metabolites in edible animal tissues. A residue definition consisting of pirimicarb only in animal tissues is proposed, although the

monitoring of this compound when used under the proposed representative use does not provide value in term of consumer safety.
The intake calculations for acute and long term exposures do not show any concern for the safety of the consumer.

Under aerobic conditions, transformations of pirimicarb in soil yields the major metabolites R34885, R31805 and R34865. Metabolite R34836 does not reaches the 10 % AR in soil but was considered relevant because contains the intact carbamate toxophore. Mineralization of pirimicarb was low and unextractable residues accounted for a maximum of 14.9 % AR after 84 d. Under dark anaerobic conditions only metabolite R31805 was found at amounts above 10 % AR.
Photolysis in soil may contribute to the environmental degradation of pirimicarb. Metabolite R34836 was the only photoproduct found at amounts above 10 % AR.
Dissipation of pirimicarb under field conditions was investigated in two field studies in California (USA) and Germany (EU). In the California field study the metabolite R35140 containing the carbamate moiety was identified at average levels of 1.98 % of applied amount. Due to the fact that it contains the carbamate moiety it is considered as a relevant metabolite for soil compartment.
Pirimicarb is medium to high persistent in soil ($DT_{50\ 20°C\ FMOC}$ = 29 – 143 d).
Evaluation Meeting (May 2004) expressed concerns on the narrow range of soil pHs tested. One MS informed that data available to their authorities contained studies performed at lower pH and that longer half-lives were observed. A data requirement was set for these studies. The references of these studies were provided by the concerned MS to the RMS during the Experts Meeting on Fate and Behaviour in the Environment (EPCO 12, September 2004). After the meeting, RMS received an evaluation document from the MS summarizing the results of three laboratory degradation studies performed in the 1970s that was included in Addendum 4 to the DAR (December 2004). Since the original reports are still not available for evaluation these results are not considered in this conclusion and the confirmatory data requirement is maintained for these studies. However, it is the opinion of the RMS that, according the summary available to them, the trend for longer DT_{50} at lower pH is not fully consistent and that no evidence of pH effects are observed in the aqueous hydrolysis study (pirimicarb stable at pH 5-9). Additionally, EFSA notes that seven of the nine values reported are within the range of half-lives obtained in the study available in the dossier. However, degradation in an additional soil would be necessary to fulfil data requirement as given in 91/414/EEC Annex II 7.1.1.2.1. RMS proposed in the DAR that since enough field studies are available, there are sufficient data for EU risk assessment. Experts meeting considered that field studies may qualitatively indicate a shorter persistence in field under bare soil conditions but no reliable DT_{50} may be obtained from them. Therefore, it is the EFSA opinion that further laboratory degradation data with an additional soil under aerobic conditions is still needed. If the studies to be submitted with respect to the data requirement set by Evaluation Meeting (see above) are finally not found acceptable to cover this data gap new data may need to be generated and provided.
The degradation of metabolites R34836, R31805 and R34865 was investigated under dark aerobic conditions. Metabolite R34836 is low to medium persistent ($DT_{50\ 20°C}$ = 7 d – 90 d), R31805 is moderately persistent ($DT_{50\ 20°C}$ = 33 d – 38 d) and R34865 is moderate to medium persistent (DT_{50}

$_{20°C}$ = 37 d – 78 d). Metabolite R34885 appears to be moderately persistent in soil ($DT_{50\ 20°C}$ = 14 d – 31 d) with data from the laboratory study performed with the parent pirimicarb.

Photolysis in soil may contribute to pirimicarb dissipation according laboratory soil photolysis.

In the field studies performed in California (USA) and Germany (EU) first order half-lives between 5 d and 46 d were calculated. Initially, RMS used field half life to calculate PEC soil. The experts meetings did not accept this because field studies were performed in bare soil and representative uses imply application to fully developed crops. It is considered that for pirimicarb photolysis may have an important role on the degradation. The contribution of this degradation route may have been overestimated in the bare soil studies with respect to the lower irradiation in the cropped field. Therefore, worst case laboratory DT_{50} = 150 d was agreed for PEC soil calculations. Consequently, the RMS has presented new PEC soil calculations in the Addendum to the DAR (December 2004).

The results of batch adsorption/desorption studies indicate that pirimicarb is low to high mobile (K_{foc} = 45 – 730 mL / g), R34836 could be classified as slightly to very high mobile (K_{foc} = 33.6 – 4320 mL / g), R34885 low to high mobile (K_{foc} = 57.2 – 867 mL / g) R31805 immobile to high mobile (K_{foc} = 130 – 80000 mL / g) and R34865 immobile to medium mobile (K_{foc} = 179 – 9650 mL / g). R31805 appears to present stronger adsorption in more acidic soils. Experts meeting considered that a dependence of the K_{foc} values on the soil clay content could be deduced and may need to be considered by MS in their assessments.

Pyrimicarb was found to be stable to hydrolysis at environmental relevant pH 5 to 9.

Photochemical degradation of pirimicarb in water under mid-European conditions is relatively rapid ($DT_{50\ (30\ cm\ depth)}$ = 12 h to 12 d). Three major photochemical metabolites were identified: R34885, R31805 and R16210.

Experts meeting considered pirimicarb to be not ready biodegradable based on water sediment study results.

A study with two water sediment systems is available. Pirimicarb partitions slowly from the water to the sediment ($DT_{50\ whole\ system}$ = 156 – 183 d; $DT_{50\ water}$ = 36 – 55 d). Degradation of pirimicarb in the sediment is very limited. Pirimicarb remained the major component in both the water and sediment compartments. Mineralization was very low with a maximum of 1.5 % of CO_2 formed after 100 d.

Surface water risk assessment presented in the DAR is based on spray drift route of entry to surface water and considered photolysis in water (DT_{50} < 1d) as the main route of dissipation.

The experts meeting discussed the environmental relevance of aquatic photolysis. Whereas acknowledging that photolysis may play an important role to the dissipation of pirimicarb in certain environmental conditions, in agreement with previous ECCO and EPCO meeting decisions, risk assessment based on a non photolysis situation must be considered for EU evaluation. Therefore, PECsw were recalculated based on the longest first order half life (DT_{50} = 55d) for the water phase of the dark water/sediment system (Addendum 4, December 2004).

Other routes of potential surface water contamination as drainage and run off were not considered in the DAR based on the presumed low persistence in soil derived from field studies results. As summarized in the soil section, persistence in soil of pirimicarb was revised based on a laboratory DT_{50} = 150 d. Therefore, potential surface water contamination through run off and drainage may not

be precluded based on the available data and surface water risk assessment may not be considered complete without addressing these other routes of potential ground water contamination.

The experts meeting identified potential for accumulation of pirimicarb into the sediment. Since no reliable half life in the sediment may be obtained from the available water sediment study, a reasonable worst case estimation was done by using DT_{50} = 335 d from the anaerobic soil degradation study. This value was used to calculate an accumulated PEC_{sed} = 29 µg / kg (Addendum 4, December 2004). However, as for the PECsw calculations this value only incorporates potential loadings through spray drift.

The potential leaching of pirimicarb and its metabolites R34836, R34885, R31805, R34865 to ground water was simulated with FOCUS PELMO 3.3.2 for the nine FOCUSgw scenarios. The geometric mean of the laboratory first order DT50s and mean K_{foc} and 1/n were used as input parameter. For pirimicarb this means that a geometric mean DT_{50} = 100.2 d was used including one value with a fitting $r^2 < 0.7$. Since only three soils were tested and of them only two fitted to first order with a $r^2 > 0.7$, worst case $DT_{50\ 20^oC\ 10\ k\ Pa}$ = 150 d should have been use for modelling purposes. However, the resulting concentration for all the nine scenarios were below 0.001 µg / L and it is not expected that the trigger 0.1 µg / L would be exceeded using a half life a 50 % longer. MS may also need to consider the K_{foc} dependence on soil clay content. Soil metabolite R35140 identified in some field studies has not been assessed for potential ground water contamination. Taking into account that the average amount found in these studies for this metabolite was of 2 % of applied dose and the structural similarities with other metabolites assessed, EFSA is of the opinion that it is very unlikely that the trigger of 0.1 µg / L would be exceeded by this metabolite. However, it needs to be properly addressed due the fact that it is more acutely toxic than the parent pirimicarb.

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

Based on the data available at the EPCO experts' meeting on ecotoxicology (EPCO 13), a high acute risk to birds from the use of pirimicarb was identified in the first tier risk assessment when calculated according to EPPO (1992). The meeting decided to seek an opinion of EFSA's Panel on Plant Health, Plant Protection and their Residues (PPR) on the principles used to refine this risk. The PPR Panel assessed the risk to birds feeding on insects in cereal fields after treatment with pirimicarb. Based on the results of this assessment, the PPR Panel is of the opinion that even at the upper limit of credible exposures, birds feeding on insects in the field are unlikely to achieve a lethal dose of pirimicarb. The short and long term risk to birds can be regarded as low if exposure is calculated according to EPPO (1992). EFSA made a first tier risk assessment available according to SANCO/4145/2000 which confirms the high acute risk to birds but also indicates a long term risk to birds. Therefore, EFSA proposes a data requirement for the notifier to submit a refinement of the long term risk to birds if the risk is assessed according to the latest guidance document (SANCO/4145/2000). For the acute risk to birds see opinion of the PPR Panel discussed above.

The acute and long term risk to mammals can be regarded as low if exposure is calculated according to EPPO (1992) and also if exposure is calculated according to SANCO/4145/2000.

The risk to aquatic organisms can be considered as high if the risk assessment is based on the standard toxicity studies with *Daphnia magna* without the presence of sediment. Risk mitigation measures need to be taken into account at MS level to address this risk. The experts' meeting (EPCO 13) decided to await the outcome of the opinion of the PPR Panel on dimoxystrobin concerning the use of a study with the presence of sediment to refine the risk. Any further refinements of the risk to aquatic organisms based on studies in the presence of sediment should be performed in accordance with the opinion of the PPR Panel on dimoxystrobin.

The experts' meeting (EPCO 13) considered the risk to bees and non target arthropods as addressed based on the available data.

The risk to soil non-target micro-organisms from pirimicarb and the metabolites R31805 and R34865 is considered to be low. It is noted by EFSA that no studies with the soil metabolites R35140, R34885 and R34836 are available. Therefore, EFSA proposes that a study or at least a solid argumentation regarding the effects of these metabolites on soil non-target micro-organisms should be made available. The need for these data was not discussed at an EPCO experts' meeting.

The risk to earthworms, soil non-target macro-organisms, non-target terrestrial plants and biological methods of sewage treatment is considered to be low.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

- Appropriate PPE as well as RPE (respiratory protective equipment) is needed in order to show an estimated operator exposure below the AOEL (refer to 2.2 and 2.12).
- Risk mitigation measure have to be taken into account at MS level to address the risk to aquatic organisms, e.g. a buffer zone of 5 metres to address the acute risk and a buffer zone of 40 metres to address the chronic risk, if the risk assessment is based on the standard toxicity studies with *Daphnia magna* without the presence of sediment. Any further refinements of the risk to aquatic organisms based on studies in the presence of sediment should be performed in accordance with the opinion of the PPR Panel on dimoxystrobin. (refer to point 5.2).

CRITICAL AREAS OF CONCERN

- Pirimicarb is proposed to be classified as toxic via oral and inhalatory exposure after single dose exposure. In relation to this fact, it should be noted that no study on repeated exposure on inhalation is submitted. Therefore, the need of respiratory protective equipment is justified. A submission of a repeated dose study might be considered at Member State level (refer to 2.2 and 2.12).
- Haematological effects and anaemia is observed at low dose levels (4 mg/kg bw/day) during repeated exposure and thus a classification of R48/22 is proposed.
- Lung tumours were evident in the mouse with a clear threshold. This is of concern but the experts could not agree whether R40 was appropriate or not.

- If the risk to birds is calculated according to the latest guidance document (SANCO/4145/2000) a long term risk to birds is observed (TER = 9.85 according to EPPO (1992) and TER= 1.91 according to SANCO/4145/2000). Therefore EFSA proposes a data requirement for the notifier to submit a refinement of the long term risk to birds if the risk is assessed according to the latest guidance document (SANCO/4145/2000).
- The risk to aquatic organisms can be considered as high if the risk assessment is based on the standard toxicity studies with *Daphnia magna* without the presence of sediment. Risk mitigation measure have to be taken into account at MS level to address the risk to aquatic organisms, e.g. a buffer zone of 5 meters to address the acute risk and a buffer zone of 40 metres to address the chronic risk. Any further refinements of the risk to aquatic organisms based on studies in the presence of sediment should be performed in accordance with the opinion of EFSA's PPR Panel on dimoxystrobin.

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

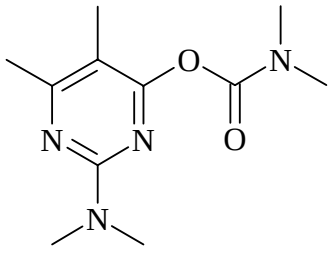
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	Pirimicarb
Function (e.g. fungicide)	Insecticide

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

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	2-dimethylamino-5,6-dimethylpyrimidin-4-yl dimethylcarbamate
Chemical name (CA) ‡	2-(dimethylamino)-5,6-dimethyl-4-pyrimidinyl dimethylcarbamate (9CI)
CIPAC No ‡	231
CAS No ‡	23103-98-2
EEC No (EINECS or ELINCS) ‡	245-430-1
FAO Specification ‡ (including year of publication)	none
Minimum purity of the active substance as manufactured ‡ (g/kg)	950 (provisional)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None
Molecular formula ‡	$C_{11}H_{18}N_4O_2$
Molecular mass ‡	238.3
Structural formula ‡	

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

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	91.6 °C
Boiling point (state purity) ‡	data requirement
Temperature of decomposition	data requirement
Appearance (state purity) ‡	White, powdery solid
Relative density (state purity) ‡	Density: 1.18 g cm^{-3} at 25°C
Surface tension	58.2 mN/m (0.999g/l solution) at 20 °C.
Vapour pressure (in Pa, state temperature) ‡	4.3 x 10^{-7} kPa at 20 °C (by interpolation)
Henry's law constant (Pa m^3 mol^{-1}) ‡	at 20 °C 3.6 x 10^{-5} Pa m^3mol^{-1} purified water 2.9 x 10^{-5} Pa m^3mol^{-1} pH 5.2 3.3 x 10^{-5} Pa m^3mol^{-1} pH 7.4 3.3 x 10^{-5} Pa m^3mol^{-1} pH 9.3
Solubility in water ‡ (g/l or mg/l, state temperature)	Purified water: 3000 mgl^{-1} pH 5.2: 3600 mg L^{-1}
	pH 7.4: 3100 mg L^{-1}
	pH 9.3: 3100 mg L^{-1}
Solubility in organic solvents ‡ (in g/l or mg/l, state temperature)	at 20 °C Heptane: 9 g/kg Octan-1-ol: 84 g/kg Ethyl Acetate: 226 g/kg Xylene: 235 g/kg Methanol: 250 g/kg Acetone: >250 g/kg Acetonitrile: >250 g/kg 1,2-Dichloroethene: >250 g/kg
Partition co-efficient (log POW) ‡ (state pH and temperature)	Purified water: 1.7 pH 7.1: 1.7
	pH 3.9: 1.1 (the applicability of the used method needs to be clarified)
Hydrolytic stability (DT50) ‡ (state pH and temperature)	pH 5, 7 and 9:<5% degradation after 30 days at 25 °C
Dissociation constant ‡	4.44 at 20 °C and pH 6.4
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	UV

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

	λ_{max} (nm) 218.8, ε (L mol^{-1} cm^{-1}) 5760 λ_{max} 244.7, ε 20900 λ_{max} 272.4, ε 855 λ_{max} 313.5, ε 3800
Photostability (DT50) ‡ (aqueous, sunlight, state pH)	Florida Summer Sunlight: DT_{50} at pH 5 and pH 7, 3.20 and 2.28 hours, respectively. Major photodegradates were R34885, R31805 and R16210 at up to 17.9%, 27.8% and 14.1% respectively at pH 5 and 16.4%, 25.5% and 26.9% at pH 7.
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	9.5×10^{-3} (Irradiation at 307-319 nm in pH 7 buffered water at 20 °C)
Flammability ‡	not classified as highly flammable
Explosive properties ‡	Pirimicarb is determined to be non-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 a.s. (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		
Wheat	South-ern Europe	Pirimor	F	Aphids	WG	50 % w/w	Tractor-mounted foliar spray	1st app: BBCH 65-77 2nd app: BBCH 83-85	1-2	Min 7 days, typical interval 14 days	-	200-300	0.21	N/A	Since growth stage is specified for second application, PHI is not appropriate
Wheat	North-ern Europe	Pirimor	F	Aphids	WG	50 % w/w	Tractor-mounted foliar spray	1st app: BBCH 65-77 2nd app: BBCH 83-85	1-2	Min 7 days, typical interval 14 days	-	200-300	0.15	N/A	Since growth stage is specified for second application, PHI is not appropriate

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)	GC, with FID
Impurities in technical as (principle of method)	GC, with FID
Plant protection product (principle of method)	GC, with FID

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	GC, BPX5 column with thermionic nitrogen specific detection. LOQ: 0.01 mg/kg for wheat grain 0.05 mg/kg for wheat straw. (LOQ refers separately to pirimicarb, R34836, R34885, R238177; common moiety method only for R34836 and R34885, no fortification experiments with R34885)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	*No analytical method is required since no MRLs are proposed/needed* GC, with NPD LOQ: 0.005 mg/kg for milk 0.01 mg/kg for tissues. (LOQ refers to pirimicarb. Method also validated for R34836 and R34885)
Soil (principle of method and LOQ)	GC, BPX-5 column with NPD, HPLC with MS/MS or fluorescence detector LOQ: 0.01 mg/kg. (LOQ refers separately to pirimicarb and R34836)
Water (principle of method and LOQ)	GC-MSD LOQ: 0.1 µg/L (surface and drinking water) (LOQ refers separately to pirimicarb, R34885, R34836, R238177; common moiety method only for R34836 and R34885, no fortification experiments with R34885))
Air (principle of method and LOQ)	GC-MSD using fragment ions LOQ: 6 µg/m^3 pirimicarb
Body fluids and tissues (principle of method and LOQ)	LC-UV (LC-MS for confirmation). LOQ: 0.05 mg/L pirimicarb (blood)

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	None

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

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Rapid-approximately 35-50% of the administered dose excreted in urine within 6 hours of dosing. Extensive-results suggest 80-90% absorption.
Distribution ‡	Widespread-highest levels mainly in liver and kidneys.
Potential for accumulation ‡	No evidence of accumulation. Highest residue levels in the liver.
Rate and extent of excretion ‡	Rapid-approximately 60-70% of the 14C-pyrimidinyl-pirimicarb excreted in urine within 24 hours of dosing, 4-10% in faeces. Approximately 70% of the 14C-carbamoyl-pirimicarb excreted in exhaled air within 24 hours of dosing, 17% in urine, 1-3% in faeces Extensive-low tissue residues together with high total recoveries.
Metabolism in animals ‡	Extensive-No parent material was detected in excreta or bile (17 identified metabolites plus unknowns).
Toxicologically significant compounds ‡ (animals, plants and environment)	Parent, R34836 (desmethylpirimicarb), R34885 (desmethylformamidopirimicarb) and 35140. *In vitro* data indicates that the plant metabolites R34836 and R34885 are rapidly metabolised intermediates in the rat. The LD_{50} values for the carbamate metabolites are in the same range as for pirimicarb or more toxic and they exhibit signs of cholinergic toxicity. Thus, they are considered to be of toxicological relevance.

Acute toxicity (Annex IIA, point 5.2)

Rat LD50 oral ‡	152 and 142 mg/kg bw in males and females, respectively-	**T; R25**
Rat LD50 dermal ‡	>2000 mg/kg bw.	
Rat LC50 inhalation ‡	0.95 and 0.86 mg/L in males and females respectively	**T; R23**
Skin irritation ‡	Slight irritant (not classified).	
Eye irritation ‡	Slight irritant (not classified).	
Skin sensitization ‡ (test method used and result)	Positive (M & K maximisation test	**R43**

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

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Red blood cells & cholinesterase inhibition **R48/22**
Lowest relevant oral NOAEL / NOEL ‡	3.5 mg/kg bw/day in females (1-yr dog study)
Lowest relevant dermal NOAEL / NOEL ‡	200 mg/kg bw/day (rat)
Lowest relevant inhalation NOAEL / NOEL ‡	No data submitted.

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	Positive in an *in vitro* mouse lymphoma assay (two metabolites also positive in the same assay). Negative in three *in-vivo* assays

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

Target/critical effect ‡	Reduced body weight and food consumption, clinical chemistry and liver and kidney effects.
Lowest relevant NOAEL / NOEL ‡	3.7 and 4.7 mg/kg bw/day in males and females, respectively (2-year rat study).
Carcinogenicity ‡	Increased incidence of benign pulmonary adenoma in mice. **R40 ?**

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Reduced body weight gain and food intake in adults and reduced foetal weight (rat).
Lowest relevant reproductive NOAEL / NOEL ‡	Parental: 21.7 mg/kg bw/day Reproduction: 81.8 mg/kg bw/day
Developmental target / critical effect ‡	Dams: deaths and reduced body weight and food consumption. Foetuses: skeletal effects.
Lowest relevant developmental NOAEL / NOEL ‡	Maternal and developmental: 10 mg/kg bw/day (rabbit)

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

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

Delayed neurotoxicity	Pirimicarb is a carbamate insecticide. There was no evidence of an effect on brain neuropathy target esterase activity in neurotoxicity studies, therefore, testing for delayed neurotoxicity was not performed.
Acute neurotoxicity (gavage administration)	NOAEL: 10 mg/kg bw
Short-term neurotoxicity (dietary administration).	Neurotoxicity NOAEL: 1000 ppm (77.1 and 84.4 mg/kg bw/day for males and females, respectively) General systemic NOAEL: 75 ppm (5.6 and 6.6 mg/kg bw/day for males and females, respectively).

Other toxicological studies ‡ (Annex IIA, point 5.8)

Metabolites, acute toxicity	R35140	79 mg/kg bw
	R31680	> 2500 mg/kg bw
	R34885	50-100 mg/kg bw
	R34836	200-400 mg/kg bw
	R31805	800-1600 mg/kg bw
	R34865	> 2000 mg/kg bw
	guanidine hydrochloride	1105 mg/kg bw
	methyl guanidine sulphate	1105 mg/kg bw
	dimethyl guanidine hydrochloride	1445 mg/kg bw
Metabolites, short term studies	R31805 is converted to R34865. The metabolites inhibit plasma cholinesterase activity at a similar dose as pirimicarb. R34836: NOAEL 5 mg/kg bw/day based on unexpected deaths at 25 mg/kg bw/day.	
	R34885 NOAEL 50 mg/kg bw/day. R31805 and R34865 NOAEL of 19.5 and 7.3 for males and females, respectively. Ames test was negative but they were mutagenic *in vitro*. However, *in vivo* UDS test was negative.	

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

Medical data ‡ (Annex IIA, point 5.9)

.....	Workers regularly had reduced plasma and erythrocyte cholinesterase activities, usually without clinical symptoms of cholinergic toxicity.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.035 mg/kg bw/day	12-month dog study.	100
AOEL ‡	0.035 mg/kg bw/day	12-month dog study.	100
ARfD ‡ (acute reference dose)	0.1 mg/kg bw	Acute neurotoxicity study.	100

Dermal absorption (Annex IIIA, point 7.3)

.....	Concentrate- 0.1% Spray dilutions- 13% based on *in vitro* human and rat comparison.

Acceptable exposure scenarios (including method of calculation)

Operator	Estimated operator exposure according to the German model indicates an exposure below the AOEL without the use of PPE (the estimated level of systemic operator exposure in this situation is equivalent to 47% of the proposed systemic AOEL of 0.035 mg/kg bw/day). According to the UK POEM the estimated exposure is below the AOEL when suitable protective gloves and respiratory protective equipment (disposable filtering facepiece respirator to EN 149 FFP2) are worn when handling the formulation and suitable protective gloves are worn when handling contaminated surfaces. The estimated level of systemic operator exposure in this situation is equivalent to 57% of the proposed systemic AOEL of 0.035 mg/kg bw/day. On the basis of these estimates, and considering the hazard classification of the formulation, the supported use of 'Aphox'/'Pirimor'

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

	(YF7904B/A10788A) will result in an estimated exposure blow the AOEL for operators wearing: • suitable protective clothing (coveralls), suitable protective gloves and suitable respiratory protective equipment (disposable filtering facepiece respirator to at least EN 149, FFP2, or equivalent) when handling the product; • suitable protective clothing (coveralls) and suitable protective gloves when handling contaminated surfaces; • suitable protective clothing (coveralls) during application. Only the supported use of Aphox/Primor 50WG on wheat, application rate 210 g pirimicarb/ha, using tractor-mounted/trailed field crop sprayers with hydraulic nozzles has been considered.
Workers	Worst case estimates using the German worker re-entry model indicate that the level of exposure to pirimicarb for an unprotected 60 kg worker in a newly treated crop will be below the AOEL (0.00819 mg/kg bw/day, equivalent to 23% of the proposed systemic AOEL of 0.035 mg/kg bw/day).
Bystanders	Assuming a concentration of 1.05 mg pirimicarb *per* ml of spray solution, no exposure reduction from clothing, the revised value of 13% dermal absorption for the spray solution, 100% absorption and retention of potential inhalation exposure, and a body weight of 60 kg; estimated total systemic bystander exposure to pirimicarb is calculated to be 0.00033 mg/kg bw (equivalent to 1% of the proposed systemic AOEL of 0.035 mg/kg bw/day) based on the simulated bystander exposure values.

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	**T;** Toxic **R23/25:** Toxic by inhalation and if swallowed; **R40?:** Limited evidence of carcinogenic effects **R43:** May cause sensitization by skin contact **R48/22** Harmful: danger of serious damage to health by prolonged exposure through inhalation

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

S2:	Keep out of the reach of children
S22:	Do not breath dust
S36:	Wear suitable protective clothing
S46:	If swallowed, seek medical advice immediately and show container or label

‡ 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	Wheat (cereals). Supporting information: lettuce (leafy vegetables), potato (root vegetables), apple (fruits) No qualitative metabolism differences between the crops.
Rotational crops	Lettuce, radish, millet
Plant residue definition for monitoring	Sum of pirimicarb, R34836 (desmethyl pirimicarb) and R34885 (desmethylformamido pirimicarb), expressed as pirimicarb
Plant residue definition for risk assessment	Sum of pirimicarb, R34836 (desmethyl pirimicarb) and R34885 (desmethylformamido pirimicarb) , expressed as pirimicarb
Conversion factor (monitoring to risk assessment)	Not relevant

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

Animals covered	Goat, Hen
Animal residue definition for monitoring	Pirimicarb only
Animal residue definition for risk assessment	Pirimicarb only
Conversion factor (monitoring to risk assessment)	Not relevant
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

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

.....	Confined rotational crop residues study at approximately 7N rate indicated total radioactive residues to be up to 1.81 mg/kg (radish leaves), of which only 4% was identified as relevant to the residue definition. Residues in succeeding crops are significantly lower than would be expected in the same directly-treated crop. No residues expected in rotational and succeeding crops

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

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

.....	Stable in wheat grain and straw for up to 12 months.

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes (beef cattle: 0.03 mg/kg bw, corresponding to 0.7 mg/kg dry feed; dairy cattle: 0.01 mg/kg bw, corresponding to 0.3 mg/kg dry feed	No	No
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	No
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	Not required	Not required	Not required
Liver	Not required	Not required	Not required
Kidney	Not required	Not required	Not required
Fat	Not required	Not required	Not required
Milk	Not required		
Eggs		Not required	

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

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

Crop	Northern or Mediterranean Region	Trials results relevant to the representative uses (a)	Recommendation/ comments	MRL estimated from trials according to the representative use	HR	STMR (b)
Wheat grain	N	8, <0.02		0.02*	<0.02	<0.02
Wheat straw	N	8, <0.02-0.38		-	0.38	0.09
Wheat grain	S	8, <0.02-0.06		0.1	0.06	<0.02
Wheat straw	S	8, 0.05-1.20		-	1.20	0.30

(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

(c) Highest residue

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

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

ADI	0.035 mg/kg bw/day
TMDI (% ADI) (according to WHO European diet)	2%
NEDI (UK diet, extreme consumers) (% ADI)	<1%, <1%, 1% and 2% for adults, children, toddlers and infants respectively.
Factors included in NEDI	STMR
ARfD	0.1 mg/kg bw
NESTI (% ARfD) according to UK large portion consumption data	<1% (Adults and Toddlers)
Factors included in NESTI calculation	No variability factor, no processing factor

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Wheat/ wheat products	No studies required. Reported total residues in wheat grain were all less than 0.06 mg/kg and generally below the LOQ.		

* 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)

Wheat	0.1 mg/kg

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

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	At 20ºC, after 112 days, 1.1-3.0%AR (3 soils). 14^{C}-pirimidinyl label.
Non-extractable residues after 100 days ‡	At 20ºC, after 112 days, 9.4-12.3%AR (3 soils). 14^{C}-pirimidinyl label.
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	R31805: up to 26.5% AR (day 168), 18.3% at day 112; R34865: up to 31.2% AR (day 372), 17.3% at day 112; R34885: up to 12.4% (day 14); R34836 (carbamate): up to 9.3% (day 140), 8.6% at day 112. ^{14}C-pirimidinyl label.

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

Anaerobic degradation ‡	At 20ºC: Mineralisation – 0.1% at day 112 Non-extractable residues - 9.4% at day 112 (1 soil). 14^{C}-pirimidinyl label. Metabolites R31805 – up to 28.5% (day 372), 11.1% at day 112 (total system). 14^{C}-pirimidinyl label.
Soil photolysis ‡	At 25ºC: Mineralisation 0.3% at day 5.2, non-extractable residues 4.4% at day 5.2. DT_{50} = 5 days (not 1st order) for irradiated in 5 day study. 94.2% AR remaining on dark controls after 5.2 days, compared with 43.9% on irradiated plates. Irradiation comparable to natural summer sunlight 30ºN. R34836 found at up to 10.2% AR (at 5.2 days sunlight equivalent). 14^{C}-pirimidinyl 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 – first order multi-compartment model used; field dissipation followed simple 1st order kinetics in two cases. Two more were √1.5st, one 2nd.

‡ 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)	**Pirimicarb** DT_{50lab} (20°C, aerobic): DT_{50} (FMOC) = 29-143 days, (3 soils, r^2 = 0.90-0.96). 1st order –10kPa values for FOCUS models: 150 days (r^2 = 0.8), 98.6 (r^2 = 0.95). **R34836** DT_{50lab} (20°C, aerobic): $DT_{50\ 20°C,\ 10kPa}$ (FMOC)= 4-65 days, (3 soils, r^2 = 0.94-0.99). $DT_{50\ 20°C,\ 10kPa}$ (1st order) = 7-90 (3 soils, r^2 = 0.71-0.96). Mean 1st order –10kPa value for FOCUS models 23.65 days. **R34885** DT_{50lab} (modelling study derived from 20°C, aerobic): 1st order t/2 = 14-31 days, (3 soils, r^2 = 0.97-0.99). Mean 1st order –10kPa value for FOCUS models 17.67 days. **R31805** DT_{50lab} (20°C, aerobic): $DT_{50\ 20°C,\ 10kPa}$ (FMOC) = 22-31 days, (3 soils, r^2 = 0.96-0.97). $DT_{50\ 20°C,\ 10kPa}$ (1st order) = 33-38 (3 soils, r^2 = 0.91-0.94). Mean 1st order –10kPa value for FOCUS models 36.25 days. **R34865** DT_{50lab} (20°C, aerobic): $DT_{50\ 20°C,\ 10kPa}$ (FMOC) = 25-64 days, (3 soils, r^2 = 0.91-1.00). $DT_{50\ 20°C,\ 10kPa}$ (1st order) = 37-78 (3 soils, r^2 = 0.74-0.94). Mean 1st order –10kPa value for FOCUS models 51.74 days. **Pirimicarb** DT_{50lab} (20°C, anaerobic): DT_{50} 335 days (1 soil, r^2 = 0.9508). Simple 1st order kinetics. DT_{50lab} (20°C, anaerobic): DT_{50} (surface water) 6.8 days (FOMC) (due to partition with soil). **Pirimicarb** DT_{90lab} (20°C, aerobic): DT_{90} (FMOC) = 256 - > 372 days, (3 soils, r^2 = 0.90-0.96). Beyond duration of study in 2 soils. 25% and 18% AR remained at end of study. **R34836** DT_{90lab} (20°C, aerobic): $DT_{90\ 20°C,\ 10kPa}$ (FMOC) = 11 - 64 days, (2 soils, r^2 = 0.94, 0.99). No value supplied for 3rd soil (beyond timescale of study of 100 d). $DT_{90\ 20°C,}$(1st order) = 22.4 – 288 d (beyond timescale of the study). R34885 No data (modelling study). **R31805** DT_{90lab} (20°C, aerobic): $DT_{90\ 20°C,\ 10kPa}$ (FMOC) = 210-632 days (beyond the timescale of study), (3 soils, r^2 = 0.96-0.97).

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

	R34865 DT_{90lab} (20°C, aerobic): $DT_{90\ 20°C,\ 10kPa}$ (FMOC) = 398-23123 days (beyond the timescale of study), (3 soils, r^2 = 0.91-1.00). **Pirimicarb** DT_{90lab} (20°C, anaerobic): DT_{90} 1113 days (extrapolated beyond the end of study from $DT_{50)}$ (1 soil, r^2 = 0.9508). Realistic worst case laboratory $DT_{50\ 20°C,\ 10kPa}$ = 150 days (simple 1st order) used for PECsoil. DT_{50lab} (10°C, aerobic): No data. Values calculated using Q_{10} factor of 2.2. DT_{50} 64 – 315 days (FOMC). Degradation in the saturated zone: no data submitted and no data required.
Field studies ‡ (state location, range or median with n value)	DT_{50f}: 4 sites (N EU at 375 g a.s./ha), single applications, parent only analysed. DT_{50}field 2 sites (simple 1st order) = 5, 13 days, r^2 = 0.85, 0.99. DT_{50}field 2 sites ($\sqrt{1.5}^{st}$ order) = 0.8, 7 days, r^2 = 0.97, 0.92. 1 site (W USA at 2.15 – 2.18 kg a.s./ha), single application, radiolabelled, metabolites sought. DT_{50}field 5 days (2nd order, r^2 = 0.99).
	DT_{90f}: DT_{90}field (N EU) = 22 – 190 days, r^2 = 0.85 - 0.97. DT_{90}field (W USA) = 46 days, r^2 = 0.99. EPCO 12: Pirimicarb degradation in these bare soil studies may be dominated by photolysis and not to be relevant for representative uses. Doubtful reliability of half lives obtained due to lack of appropriate validation data to support the LOQ claimed for the analytical method employed.
Soil accumulation and plateau concentration ‡	No data supplied. Calculation provided by RMS in addendum 4 and List of end points under /PEC soil.

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	**Pirimicarb** K_{foc} = 45-730 ml/g (mean 290 ml/g), 4 soils, pH 5.3-7.9, %oc 0.8-6.0. Freundlich coeff. (1/n) = 0.79-0.91 (mean 0.85). No pH relationship observed. **R34836** K_{foc} = 33.6-4320 ml/g (mean 927 ml/g), 6 soils, pH 5.3-8.0, %oc 0.3-3.6. Freundlich coeff. (1/n) = 0.83-0.93 (mean 0.90). No pH relationship observed. **R34885** K_{foc} = 57-867 ml/g (mean 269 ml/g), 6 soils, pH 5.3-8.0, %oc 0.3-3.6. Freundlich coeff. (1/n) = 0.90-0.95 (mean 0.92). No pH relationship observed. **R31805** K_{foc} = 130-80000 ml/g (mean 14873 ml/g), 6 soils, pH 4.4-7.9, %oc 0.5-5.1. Freundlich coeff. (1/n) = 0.90-0.95 (mean 0.92). Appears to be pH dependent, with stronger adsorption occurring in more acidic soils. **R34865** K_{foc} = 179-9650 ml/g (mean 2940 ml/g), 6 soils, pH 5.3-8.0, %oc 0.3-3.6. Freundlich coeff. (1/n) = 0.62-0.85 (mean 0.76). No pH relationship observed. EPCO 12: In general for metabolites the highest Kfoc value corresponds to the soil with highest clay content. Mean Kfoc and 1/n values used for pirimicarb and metabolites in $FOCUS_{GW}$ 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 ‡	No data submitted, none required.
Lysimeter/ field leaching studie ‡	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	50% interception, soil density 1.5 g/ml, top 5 cm soil layer, 1st order DT50 (laboratory) 150 days. For metabolites no degradation between applications is assumed.
Application rate	2 x 210 g a.s./ha with 7 day spray interval. This represents S EU regime on wheat.

$PEC_{(s)}$ mg/kg	**Parent 2x210g/ha Actual**	**Parent 2x210g/ha Time Weighted Average**	**R34836[a]**	**R34885[b]**	**R31805[c]**	**R34865[d]**
Initial (after 2nd application)	0.276	0.276	0.016	0.037	0.052	0.056
Short term 24h	0.274	0.275				
2d	0.273	0.275				
4d	0.270	0.273				
Long term 7d	0.267	0.271				
28d	0.242	0.258				
50d	0.219	0.246				
100d	0.174	0.221				
Peak accumulated PEC soil	0.338 mg/kg occurring after 4 year of application. Steady state before application will be 0.198 mg/kg.					

[a]Formed at max 5.9% AR (field data)
[b]Formed at max 12.4% AR (lab data)
[c]Formed at max 26.5% AR (lab data)
[d]Formed at max 31.2% AR (lab data)

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: At 25ºC, with 32 days incubation, no significant degradation of a.s. detected. pH_7: At 25ºC, with 32 days incubation, no significant degradation of a.s. detected. pH_9: At 25ºC, with 32 days incubation, no significant degradation of a.s. detected.

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

Photolytic degradation of active substance and relevant metabolites ‡	Quantum yield aqueous photolysis studies half-life (30 cm depth) = 0.5 days (Summer), 12 days (Winter) using Frank and Klöpffer model. 24 hour aqueous photolysis (pH5 and pH7) using simulated sunlight (30ºN), 5cm path length, half life = 2.6 hours pH5, 1.9 hours pH 7 (r^2 = 0.99, 0.98). 3 metabolites (R34885, R31805, R16210) at >10% AR. R34885 - max 17.9% pH5, 16.4% pH7 R31805 - max 27.8% pH5, 25.5% pH7 R16210 - max 14.1% pH5, 26.9% pH7
Readily biodegradable (yes/no)	No data submitted, none required. A.s. assumed not to be ready biodegradable.
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡ - DT_{50} whole system ‡ - DT_{90} whole system ‡ Mineralization Non-extractable residues	Aerobic lab sediment/water at 20°C, (to SETAC EU guideline) in two systems (natural water and sediment). DT_{50} = 17 – 25 days (water, √1.5st and 1.5st order, r^2 0.99 both systems); 1st order DT_{50} (water) 36 - 55 days (r^2 0.93 - 0.87), 1st order DT_{90} (water) 156 - 183 days, total system 1st order DT_{50} =156 - 185 days (r^2 0.894 - 0.740), total system 1st order DT_{90} = 518 - 615 days. **Whole system DT_{50} are not found neither in the DAR or any addendum** Sediment DT_{50} not calculated, as pirimicarb concentrations still increasing at end of study. No major (> 10% AR) metabolites identified.
Distribution in water / sediment systems (active substance) ‡	Pirimicarb - Volatiles 0.8 and 1.5% (100 days). Pirimicarb - Unextractables 9.6% and 13.4% (100 days).
Distribution in water / sediment systems (metabolites) ‡	Pirimicarb distribution - At 100 days: 22.6% and 13.3% parent in water; 40% and 48% in sediment.

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

Parent

Method of calculation	Overall 90th %ile (1 application), 82nd %ile (2 applications) spray drift values at 1 m, water 1st order $DT_{50\ water}$ = 55 d, 1 crop, 30cm deep water body. *Pirimicarb will degrade between applications. However, metabolites R34836, R34885 and R35140 have been considered as they contain the carbamate moiety. PEC_{sw} expressed as total carbamate residue.

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

Application rate	Wheat: 2 x 210 g a.s./ha, 7 day application interval (S Europe).
Main routes of entry	Spray drift

Instantaneous PECsurface water for pirimicarb residue (µg/l) for wheat, from spray drift at 1 metre

Days after 2nd treatmen	Actual µg/L	TWA µg/L
0	3.191	3.191
1	3.151	3.171
2	3.112	3.151
4	3.034	3.112
7	2.922	3.055
14	2.675	2.926
21	2.449	2.804
28	2.242	2.689
42	1.880	2.478

These PEC are higher than the initial PEC following a single treatment using a single 90th percentile spry drift 1m of 2.77 %.

To assess situations were irradiation and photolyis is relevant PECsw of total carbamate residue will be 2.18 µg/L including pirimicarb and metabolite R31805.

PEC (sediment)

Parent

Method of calculation	From spray drift values, with same assumptions as for PECsurface water. Assumes all pirimicarb partition to sediment, sediment depth 5cm, density 1.3 g/ml, no dissipation.
Application rate	For wheat – see above.

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

PECsediment of a.s. and total carbamate residue (µg/kg) for wheat from spray drift at 1 metre

Multiple applications
15.4 µg/kg after a single years application 29 µg/kg after ten years of use (pseudo PECsw for use in sediment dwellers risk assessment would be 6.282 µg/L)

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	FOCUSgw modelling – used model FOCUS-PELMO 3.3.2, for all 9 scenarios, according to all FOCUSgw guidance. Crop: wheat. DT_{50} from geometric mean lab study, normalised to 20ºC and -10kPa. **Pirimicarb:** DT_{50} 100 days, mean Kfoc 290 ml/g, mean Freundlich coeff. (1/n) 0.85. After Peer review EFSa propose to use 150 d (in agreement with FOCUSgw guidelines. No dramatic impact in the results expected. **R34836** DT_{50} 24 days, mean K_{foc} 927 ml/g, mean Freundlich coeff. (1/n) 0.90. **R34885** DT_{50} 18 days, mean K_{foc} 269 ml/g, mean Freundlich coeff. (1/n) 0.92. **R31805** DT_{50} 36 days, mean K_{foc} 14873 ml/g, mean Freundlich coeff. (1/n) 0.92.pH dependence not considered in the calculation. **R34865** DT_{50} 52 days, mean K_{foc} 2940 ml/g, mean Freundlich coeff. (1/n) 0.76.
Application rate	S Europe: 21 g a.s./ha (210 g a.s./ha with 90% crop interception), applied 33 days and 26 days before harvest. N Europe: 15 g a.s./ha (150 g a.s./ha with 90% crop interception), applied 40 days and 33 days before harvest.

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

PEC$_{(gw)}$

Maximum concentration	Not reported
Average annual concentration (Results quoted for modelling with FOCUSgw scenarios, according to FOCUS guidance)	<0.001 µg/l all scenarios and all metabolites.

PEC(gw) - FOCUS modelling results

Scenario (all wheat)	Parent (µg/l)	Metabolite (µg/l)			
		R34836	R34885	R31805	R34865
Châteadun	<0.001	<0.001	<0.001	<0.001	<0.001
Hamburg	<0.001	<0.001	<0.001	<0.001	<0.001
Jokioinen	<0.001	<0.001	<0.001	<0.001	<0.001
Kremsmünster	<0.001	<0.001	<0.001	<0.001	<0.001
Okehampton	<0.001	<0.001	<0.001	<0.001	<0.001
Piacenza	<0.001	<0.001	<0.001	<0.001	<0.001
Porto	<0.001	<0.001	<0.001	<0.001	<0.001
Sevilla	<0.001	<0.001	<0.001	<0.001	<0.001
Thiva	<0.001	<0.001	<0.001	<0.001	<0.001

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	9.5 x 10^{-3}
Photochemical oxidative degradation in air ‡	DT50 = <1 hour (Atkinson calculation).
Volatilization ‡	From leaf surface: 47.4% recovery AR (24hours) [1]. From soil: 89.5% recovery AR (24 hours)[1]. Vapour pressure: 4.3 x 10^{-7} kPa @ 20°C Henrys Law constant: 3.6 x 10^{-5} Pa.m^3.mol^{-1} @ 20°C (purified water)

[1]Light not excluded from study; photolysis may have contributed to dissipation.

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: pirimicarb, R34885[30], R34836[31], R31805[32], R34865[33], R35140[34]. Definitions for monitoring: pirimicarb, R34885 (pending on assessment on effects on soil non-target micro-organisms), R34836 (pending on assessment on effects on soil non-target micro-organisms), R35140 (pending on assessment on effects on soil non-target micro-organisms). **Water** **Ground water** Definitions for risk assessment: pirimicarb, R35140 (to be assessed for potential ground water contaminations) Definitions for monitoring: pirimicarb, R35140 (to be assessed for potential ground water contaminations) **Surface water** Definitions for risk assessment: pirimicarb (water and sediment), R34885, R31805, R16210[35] (photolysis metabolites). Definitions for monitoring: pirimicarb **Air** Definitions for risk assessment: pirimicarb Definitions for monitoring: pirimicarb

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

[30] R34885: 5,6-dimethyl-2-(methylformamido) pyrimidin-4-yl dimethylcarbamate
[31] R34836 : 5,6-dimethyl-2-(methylamino) pyrimidin-4-yl dimethylcarbamate
[32] R31805: 2-dimethylamino-5,6-dimethylpyrimidin-4-ol
[33] R34865: 5,6-dimethyl-2-(methylamino) pyrimidin-4-ol
[34] R35140: 2-amino-5,6-dimethylpyrimidin-4-yl dimethylcarbamate
[35] R16210: 1,1-dimethylguanidine

‡ 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 fate and behaviour data	Not ready 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

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

Acute toxicity to mammals ‡	LD_{50}: 20.9 mg a.s./kg bw (*Colinus virginianus*)
Acute toxicity to birds ‡	LC_{50}: 1805 ppm (≡ 394 mg a.s./kg bw/day) (*Colinus virginianus*)
Dietary toxicity to birds ‡	NOEC: 60 ppm (≡ 12.1 mg a.s./kg bw/day) (*Anas platyrhynchos*)
Reproductive toxicity to birds ‡	LD_{50}: 142 mg a.s./kg bw (female rat)
	NOEC: 750 ppm (≡ 81.8 mg a.s./kg bw/day) (rat multigeneration study)

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.21	Wheat	small insectivorous bird consuming small insects	acute	**4.77**	10
0.21	Wheat	small insectivorous bird consuming small insects	short term dietary	296	10
0.21	Wheat	small insectivorous bird consuming small insects	long term/ reproductive	9.85	5
0.21	Wheat	small insectivorous mammal consuming large insects	acute	346	10
0.21	Wheat	small insectivorous mammal consuming large insects	long term/ reproductive	1323	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/L)
Laboratory tests ‡				
cold water fish *Oncorhynchus mykiss*	technical pirimicarb	96 h, static	LC_{50}	79

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
warm water fish *Pimephales promelas*	technical pirimicarb	96 h, static	LC_{50}	>100
invertebrate *Daphnia magna*	technical pirimicarb	48 h, static	EC_{50}	0.017
green alga *Pseudokirchneriella subcapitata*	technical pirimicarb	96 h, static	E_bC_{50} E_rC_{50}	140 180
invertebrate *Daphnia magna*	500 g/kg WG (YF7904B)	48 h, static	EC_{50}	0.024
cold water fish *Oncorhynchus mykiss*	metabolite R34865	96 h, static	LC_{50}	>120
invertebrate *Daphnia magna*	metabolite R35140	48 h, static	EC_{50}	0.09
invertebrate *Daphnia magna*	metabolite R34836	48 h, static	EC_{50}	0.056
invertebrate *Daphnia magna*	metabolite R34885	48 h, static	EC_{50}	0.018
invertebrate *Daphnia magna*	metabolite R31805	48 h, static	EC_{50}	>100
invertebrate *Daphnia magna*	metabolite R34865	48 h, static	EC_{50}	>120
invertebrate *Daphnia magna*	metabolite R16210	48 h, static	EC_{50}	28
green alga *Pseudokirchneriella subcapitata*	metabolite R34865	72 h, static	E_bC_{50}: E_rC_{50}:	>120 >120
green alga *Pseudokirchneriella subcapitata*	metabolite R31805	72 h, static	E_bC_{50}: E_rC_{50}:	>120 >120
Chronic and higher-tier laboratory tests				
cold water fish *Oncorhynchus mykiss*	technical pirimicarb	28 d, flow-through	NOEC	<18
warm water fish *Pimephales promelas*	technical pirimicarb	36 d, flow-through	NOEC	10
invertebrate *Daphnia magna*	technical pirimicarb	21 d, semi-static	NOEC	0.0009

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
invertebrate *Daphnia magna*	technical pirimicarb	10 d, static, in presence of sediment	EC_{50}: NOEC	>0.015 0.006
Additional invertebrate species tests				
Daphnia pulex	technical pirimicarb	48 h, static	LC_{50}	0.011-0.033
Macrocyclops fuscus	technical pirimicarb	48 h, static	EC_{50}	35
Calanoid copepods	technical pirimicarb	48 h, static	LC_{50}	>0.9
Gammarus pulex	technical pirimicarb	48 h, static	EC_{50}	48
Asellus aquaticus	technical pirimicarb	48 h, static	EC_{50}	120
Hyalella azteca	technical pirimicarb	48 h, static	EC_{50}	52
Crangonyx pseudogracilis	technical pirimicarb	48 h, static	EC_{50}	44
Ostracoda	technical pirimicarb	48 h, static	EC_{50}	32
Cloeon dipterum	technical pirimicarb	48 h, static	LC_{50}	>0.9
Ischnura elegans	technical pirimicarb	48 h, static	EC_{50}	88
Chaoborus crystallinus	technical pirimicarb	48 h, static	EC_{50}	42
Notonecta glauca	technical pirimicarb	48 h, static	LC_{50}	>0.9
Notonecta triguttata	technical pirimicarb	48 h, static	LC_{50}	>40
Eretes sticticus	technical pirimicarb	48 h, static	LC_{50}	>40
Micronecta sedula	technical pirimicarb	48 h, static	LC_{50}	62
Sigara substriata	technical pirimicarb	48 h, static	LC_{50}	53
Orthetrum albistylum	technical pirimicarb	48 h, static	LC_{50}	>40

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Sympterum frequens	technical pirimicarb	24 h, static	LC_{50}	>40
Tetrahymena pyriformis	technical pirimicarb	24 h, static	EC_{50}	370
Erpobdella	technical pirimicarb	48 h, static	EC_{50}	110
Dugesia	technical pirimicarb	48 h, static	EC_{50}	140
Planorbidae	technical pirimicarb	48 h, static	EC_{50}	200
Lymnaea stagnalis	technical pirimicarb	48 h, static	EC_{50}	19
Sediment-dwelling organisms				
Chironomus riparius	technical pirimicarb	48 h, static	EC_{50}	>10
Chironomus riparius	technical pirimicarb	48 h, static	EC_{50}	60

Microcosm or mesocosm tests
None submitted

* Some of the additional species data are from studies of uncertain validity and in themselves may not be considered essential. However, the whole data set is used to identify *Daphnia* as the key sensitive organisms and thus reduce the uncertainty factor applied to acute and chronic risk assessments for all aquatic invertebrates (see Addendum 1 to the DAR).

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
Standard acute laboratory tests						
2 x 0.21	Wheat	*Oncorhynchus mykiss*	96 h, static	1m	24765	100
		Daphnia magna	48 h, static	1 m	**5.33***	10*
				5 m	**27**	10*
		Selenastrum capricornutum	96 h, static	1 m	46887	10
Chronic and higher-tier laboratory tests						
2 x 0.21	Wheat	*Pimephales promelas*	36 d, flow-through	1 m	3135	10

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
		Daphnia magna	21 d, semi-static	1 m	**0.28**	10
				5 m	**1.43**	10
				40 m	11.2	10
Additional invertebrate species tests						
TERs for all of the additional non-daphnid invertebrates tested have not been included here, they were all >100 at 1 m drift (range >410-170000).						

*In consideration of species sensitivity in light of additional species testing the EPCO 13 Expert meeting on ecotoxicology accepted to lower the Annex VI trigger value from 100 to 10.

Bioconcentration

No bioconcentration study is required according to Annex III Point 8.2.3, as the log Pow of pirimicarb (1.7) and major metabolites is <3.

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

Acute oral toxicity ‡	technical pirimicarb (24 h LD_{50}): 4.0 µg a.s./bee 50% w/w WG 'JF4122B' (24 h LD_{50}): ≡ 4.4 µg a.s./bee YF7904B ≡ 14 µg a.s./bee
Acute contact toxicity ‡	technical pirimicarb (24 h LD_{50}): 53.1 µg a.s./bee ≈50% w/w WG 'JF4122B' (24 h LD_{50}): ≡ 51.1 µg a.s./bee

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.21	wheat	a.s. oral	52.5	50
0.21	wheat	a.s. contact	3.95	50
0.21	wheat	form.n oral	47.7	50
0.21	wheat	form.n contact	4.1	50

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

Field or semi-field tests An assessment of various higher tier field trials has demonstrated that applications of pirimicarb at rates up to and above the maximum representative use rate of 210 g a.s./ha did not result in adverse effects on honeybees. Pirimicarb also has no properties which would indicate any residual or brood toxicity.

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

Species	Test duration and type	Test Substance	Endpoint	Value/effect (g a.s./ha)	Annex VI Trigger
Laboratory dose-response tests					
Predatory mite *Typhlodromus. pyri*	14-day extended laboratory test on bean leaf discs	'YF7904B' (500 g a.s./kg WG)	7-day LR_{50}: 14-day no significant effect on fecundity: & mortality:	835 750 250	-
Aphid parasitoid *Aphidius rhopalosiphi*	16-day extended laboratory test on barley seedlings	'YF7904B' (500 g a.s./kg WG)	48h LR_{50}: 48h LR_{30}: 14-day no stat. significant effect: (mortality & fecundity)	620 419 250	-
Green lacewing *Chrysoperla carnea*	extended laboratory test, larvae exposed for up to 18d on apple leaves, fecundity of adults assessed over 15d	'YF7904B' (500 g a.s./kg WG)	LR_{50}: no apparent effect on fecundity: & mortality:	N/A 750 140	-
Hoverfly *Episyrphus balteatus*	extended laboratory test, larvae exposed on broad bean seedlings for 21d, adult fecundity assessed after 2 weeks	'YF7904B' (500 g a.s./kg WG)	LR_{50}: no 'significant' effect on fecundity: & pre-imaginal mortality:	14.6 60 2 (based on 18% pre-imaginal mortality)	-
Laboratory limit tests					
Aphid parasitoid *Aphidius rhopalosiphi*	16 day extended limit test on wheat seedlings, 48 hr exposure of adults followed by fecundity test	'YF7904B' (500 g a.s./kg WG)	effects on adult mortality and reproduction at maximum rate equivalent to 140g a.s./ha	no repellency, mortality or effect on reprod.n at 140 g a.s./ha	30% effect

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

Species	Test duration and type	Test Substance	Endpoint	Value/effect (g a.s./ha)	Annex VI Trigger
Lycosid spider *Pardosa* spp.	6 day extended laboratory limit test on soil	'YF7904B' (500 g a.s./kg WG)	effects on adult mortality and feeding activity at maximum rate equivalent to 140g a.s./ha	no statistically significant effect seen at 140 g a.s./ha	30% effect
Carabid beetle *Pterostichus melanarius*	6 day extended laboratory limit test on soil	'YF7904B' (500 g a.s./kg WG)	effects on adult mortality and feeding activity at maximum rate equivalent to 140g a.s./ha	no statistically significant effect seen at 140 g a.s./ha	30% effect
Hoverfly *Episyrphus balteatus*	16 day extended laboratory test on broad bean seedlings	'YF7904B' (500 g a.s./kg WG)	effects on larval mortality and larval and pupal weights at rates equivalent to 75 and 150g a.s./ha	**58**% and **54**% corrected mortality at 75 and 150 g a.s./ha respectively; no stat. sig. effect on weight of any surviving larvae/pupae	30% effect
Field or semi-field tests A number of field studies have shown that under more realistic conditions the direct effects of pirimicarb on non-target arthropods are low. Most of the impacts seen could be attributed to reductions in the numbers of aphid prey/hosts. The particular sensitivity of syrphids seen in laboratory studies was also reported in field studies where recovery was not clearly demonstrated. However, further information supplied by the Notifier has indicated that residue dissipation on foliage should permit syrphid populations to recover once their larval food increases.					

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

Acute toxicity ‡	Pirimicarb 50% WG 'YF7321A'(14 day LC_{50}): >120 mg product/kg soil (≡ >60 mg a.s./kg)
	R31805 metabolite (14 day LC_{50}): >1000 mg/kg
	R34865 metabolite (14 day LC_{50}): >1000 mg/kg
Reproductive toxicity ‡	None submitted and not considered necessary

Field studies

In a 5-year grassland field study, with pirimicarb applied at least twice per year at between 0.28 and 5 kg a.s./ha, no consistent differences were observed between treatment and control plots. Earthworm populations were not adversely affected by pirimicarb applications at up to 5 kg a.s./ha.

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

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
2 x 210	Wheat	Acute	> 178	<10

Effects on other soil macro-organisms involved in organic matter breakdown (Annex IIIA, point 10.6.2)

No additional data submitted. A low risk is predicted due to assessment of the levels and persistence of pirimicarb its and metabolites in soil, plus consideration of their effects on earthworms, non-target arthropods and soil microbial processes.

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

Nitrogen mineralization	(formulated pirimicarb)	'YF7321A' (50% w/w WG): No significant effect >25% at equivalent of up to 5.0 mg a.s./kg soil
Carbon mineralization	(formulated pirimicarb)	'YF7321A' (50% w/w WG): No significant effect >25% at equivalent of up to 5.0 mg a.s./kg soil
Nitrogen mineralization	(R31805 metabolite)	No significant effect >25% at up to 1.75 mg a.s./kg soil
Carbon mineralization	(R34865 metabolite)	No significant effect >25% at up to 1.61 mg a.s./kg soil

Effects on other non-target organisms (flora and fauna) believed to be at risk (Annex IIA, point 8.6)

The effects of pirimicarb on seedling emergence, subsequent plant development and vegetative vigour were investigated in two glasshouse studies on a range of monocotyledonous and dicotyledonous plants. None of the species tested showed any significant adverse pre-or post-emergence effects after application of pirimicarb at 791 g a.s./ha.

Classification and proposed labelling (Annex IIA, point 10)

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

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

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median

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