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

dichlorvos

finalised: 12 May 2006

SUMMARY

Dichlorvos is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[1], as amended by Commission Regulation (EC) No 1490/2002[2]. This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

Italy being the designated rapporteur Member State submitted the DAR on dichlorvos in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 20 October 2003. Following a quality check on the DAR, the peer review was initiated on 21 June 2004 by dispatching the DAR for consultation of the Member States and the sole applicant Denka International B.V. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting on 9 February 2005. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in June and July 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 5 April 2006 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide comprise room treatment (by using fogging vaporising equipment) to protect flower bulbs from thrips. The application rate is 2.2 g dichlorvos per 100 m³ with maximal 3 applications resulting in a maximum total dose of 6.6 g/100 m³. Dichlorvos can be used as acaricide and insecticide. It should be noted that the applicant stated that only the use as insecticide will be supported in the EU review programme.
The representative formulated product for the evaluation was "Dichlorvos 550 g/L EC", an emulsifiable concentrate (EC), registered in some Member States of the EU.

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

No methods are available to monitor the compounds given in the respective residue definition for soil water and air.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that at least limited quality control measurements of the plant protection product are possible.

Dichlorvos is toxic following acute oral and dermal exposure and very toxic after acute inhalation exposure. It is expected to be slightly irritating to the skin and eyes. Dichlorvos was found to have a skin sensitizing potential. The following classification was proposed: R25 Toxic if swallowed, R24 Toxic in contact with skin, R26 Very toxic by inhalation, R43 May cause sensitization by skin contact. Dichlorvos did not pose any concern for reproductive and developmental toxicity. Based on the available data, no delayed neuropathy was observed. A question addressing the mutagenic and carcinogenic potential of dichlorvos was proposed to be forwarded to the EFSA PPR panel due to the weaknesses of data provided, not adequate to exclude carcinogenic activity. Therefore information and expertise was considered insufficient for the setting of reference values and accordingly the operator exposure calculations, was not considered appropriate until the outcome of the EFSA PPR panel discussions. The PPR opinion[3] has been adopted on 1 April 2006. Taking the conclusions in the opinion into consideration it was agreed at the meeting with Member State's representatives in April 2006 that the risk assessment is still inconclusive due to the uncertainties of the genotoxic and carcinogenic properties of dichlorvos also considering the overall poor quality of the dossier.

The evaluation of the residue behaviour of dichlorvos in plants and livestock animals and a dietary risk assessment for consumers is not relevant for the representative use.

The evaluation of the environmental fate and behaviour of dichlorvos in soil and natural surface water systems is not relevant for the representative use as these environmental compartments will only be exposed following an accident with or misuse of the plant protection product. When appropriate horticultural practice is followed, flower bulbs are washed before treatment. Therefore unlike post harvest storage treatments of other plant products, dichlorvos contamination of surface water via wash water will not occur. Based on its vapour pressure, this liquid active substance is volatile and based on its dimensionless Henry's Law air water partition coefficient (1.06×10^{-5} at 20°C) it will be moderately volatile from aqueous systems. Therefore from the representative indoor use, exposure of air may occur when stores are vented after treatment, however wet and dry re-deposition to land and surface waters would be expected to be negligible. Dichlorvos would not be expected to be subject to long range transport, as in the upper atmosphere photochemical reaction with hydroxyl radicals is estimated to result in a half life of 13-20 hours.

[3] 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 dichlorvos in the context of Council Directive 91/414/EEC (Question N° EFSA-Q-2005-246). *The EFSA Journal* (2006) 343, 1-45.
http://www.efsa.europa.eu/science/ppr/ppr_opinions/1452_en.html

The risk to birds and mammals, aquatic organisms, bees, other non-target arthropods, earthworms and other non target organisms, soil non-target micro-organisms was considered as low because exposure is assumed to be negligible for the representative indoor use in flower bulbs. The risk posed to biological methods of sewage treatment was assessed as low.

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

TABLE OF CONTENTS

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. Dichlorvos is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating Italy as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Italy submitted the report of its initial evaluation of the dossier on dichlorvos, hereafter referred to as the draft assessment report, to the EFSA on 20 October 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 21 June 2004 to the Member States and the main applicant Denka International B.V. as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 9 February 2005 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier attended this meeting.

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

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 5 April 2006 leading to the conclusions as laid down in this report.

Following the consultation of technical experts a question relating to the mutagenic and carcinogenic properties was forwarded to the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR), which was addressed by an opinion, adopted 1 of April 2006 (for full reference see footnote page 2).

In accordance with Article 8(7) of the amended Regulation (EC) No 451/2000, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received
- the resulting reporting table (rev. 1-1 of 4 March 2005)
- the consultation report

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation
- the evaluation table (rev. 2-2 of 9 May 2006)

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

Dichlorvos is the ISO common name for 2,2-dichlorovinyl dimethyl phosphate (IUPAC).

Dichlorvos belongs to the class of organophosphate acaricides and insecticides such as monocrotophos and naled. Dichlorvos is a contact and respiratory insecticide with a fast knock-down effect on most flying insects and acts as an acetyl cholinesterase inhibitor.

The representative formulated product for the evaluation was "Dichlorvos 550 g/L EC", an emulsifiable concentrate (EC), registered in some Member States of the EU.

The evaluated representative uses as insecticide comprise room treatment (by using fogging vaporising equipment) to protect flower bulbs from thrips. All other uses were withdrawn during the evaluation of the dossier and therefore not peer reviewed. The application rate is 2.2 g dichlorvos per

100 m³ with maximal 3 applications resulting in a maximum total dose of 6.6 g/100 m³. Dichlorvos can be used as acaricide and insecticide. It should be noted that the applicant stated that only the use as insecticide will be supported in the EU review programme.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

At the moment no minimum purity of dichlorvos as manufactured can be given, because further clarification is needed. It seems that on Member State level different data than the one in the EU dossier were submitted. However, according to the FAO specification 11/TC/S (1989) the minimum purity should not be less than of 950 g/kg. Nevertheless, the data which were submitted to at least one Member State support based on current batches a higher minimum purity. In addition, clarification is necessary with respect to the proposed maximum content of the significant impurities.
Therefore, it is not possible to propose a specification for the technical material.
The technical material contains chloral, which has to be regarded as relevant impurity. The maximum content in the technical material should not be higher than 5 g/kg (FAO 11/TC/S, 1989). However, it should be pointed out that no data were supplied by the applicant to either confirm or refute the relevance of this impurity.

The content of dichlorvos in the representative formulation is 550 g/L (pure).

Beside the specification, the assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of dichlorvos or the respective formulation. However, the following data gaps were identified:

- spectra for the relevant impurity chloral and UV data for dichlorvos
- a study for the determination of the auto-flammability
- a study for the determination of the explosive properties of dichlorvos and possibly for the representative formulation
- a study for the hydrolysis of dichlorvos
- a shelf-life study to demonstrate that the relevant impurity chloral in the technical material is not increasing in the formulation upon storage
- information on one certain formulant in the representative formulation
- data on the pH value of the representative formulation

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

The assessment of the data package revealed the following data gaps with respect to the analytical methods:

- validated analytical methods for the determination of impurities in the technical material
- validated analytical methods for the determination of dichlorvos in soil, water, air as well as animal tissues and blood.

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

No methods are available to monitor the compounds given in the respective residue definition, i.e. dichlorvos in soil, water and air.
Analytical methods for food of plant and animal origin are not required due to the fact that no residue definition is proposed (see chapter 3).
With respect to the analytical method for the determination of residues in tissues and blood to cover Annex point 4.2.5 of the Directive 96/46/EC, it should be noted that the applicant is trying to develop an appropriate method, but for the moment it seems that all analytes are transient or non specific for dichlorvos (EFSA was informed by the applicant via email).

The discussion in the meeting of experts (EPCO 30, July 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material, certain physical, chemical and technical properties of the dichlorvos and the representative formulation as well as to certain analytical methods.

Recently submitted studies, regarding the hydrolysis and the UV spectra of dichlorvos and the pH value of the representative formulation (September 2005) were neither peer reviewed by other MS nor discussed in an EPCO meeting of experts. The assessment of the rapporteur Member State is given only in the evaluation table (17433/EPCO/BVL/04 rev. 2-0; 11.11.2005).

2. Mammalian toxicology

Dichlorvos was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 23) in June 2005. During the process, both the rapporteur Member State and MS found it difficult to assess the dossier due to the poor quality of the data package. Initially, in the DAR, the rapporteur Member State indicated several data requirement for new studies to be submitted in addition to the concern in relation to the genotoxic and carcinogenic properties. The information and expertise was considered insufficient for the setting of reference values (tentative values were set) therefore the risk assessment was considered inconclusive.
At the experts´ meeting, the conclusions drawn by the rapporteur Member State were generally supported and thus no final risk assessment could be concluded. The question on the mutagenic and carcinogenic properties, whether a threshold was possible to identify as well as the question of

relevance for human toxicity, of dichlorvos was forwarded to the PPR panel. The questions raised from the EFSA/EPCO peer review process were

1) **Related to the increased incidence of tumours observed in various tissues in rats and mice following dichlorvos exposure, is it possible to identify a mode of action (for any of the tumours) and in that case, is it possible to set a threshold?**
2) **Considering the modes of action of the tumourigenic responses are any of them relevant for humans?**

Below is a summary of the conclusion of the adopted opinion of the PPR Penel[4] (EFSA-Q-2005-246).

Question 1

Mode of action on genotoxicity:

The PPR panel concludes that based on the available data there are clear indications that dichlorvos is an *in vitro* mutagen. The panel states that although the *in vivo* studies show some deficiencies there are evidence that dichlorvos is a weak DNA alkylating agent. Many of studies suffer from methodological or reporting deficiencies and no specific study is provided to demonstrate to alkylating potential. The panel concludes that there is limited evidence for that dichlorvos is a site of contact *in vivo* mutagen.

Mode of action on carcinogenicity:

The panel concludes that tumours observed in rat are not compound related whereas the forestomach tumours observed in mouse are. However, as the dose was higher in the mouse, the lack of response in the rat could be due to lower doses rather than species differences. The tumours in the forestomach are considered as a site of contact effect (route of exposure gavage). It is possible that dichlorvos modifies DNA in the cells at site of contact which results in a mutagenic response and leads to tumours at this site. Further on, it is concluded that another mode of action might be plausible but strong evidence were lacking. If, the mode of action is via DNA reactivity, it might be possible to assume that other tumours could be produced at other sites following systemic exposure. However, the dose would be high and at a level of inducing severe systemic toxicity as well. Thus, the panel concluded that it was possible to set a threshold.

Question 2

The Panel concludes that the forestomach is a unique structure for the rodent as compared to human stomach. As it was not possible to exclude DNA interaction as a critical step this would be as a cause of the high local concentration. There are substantial scientific uncertainty in relation to the mode of action and relevance for humans. The weight of evidence suggest that this would not occur at there

[4] 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 dichlorvos in the context of Council Directive 91/414/EEC (Question N° EFSA-Q-2005-246). *The EFSA Journal* (2006) 343, 1-45. http://www.efsa.europa.eu/science/ppr/ppr_opinions/1452_en.html

EFSA notes: Following the outlines of the conclusion given in the PPR panel opinion (EFSA-Q-2005-246) it is plausible to assume that for forestomach tumours in the mouse a threshold can be set and the relevance for humans are low depending on the unique structure of forestomach in relation to human stomach. Furthermore, tumour formation occurs at high concentrations which should be considered in relation to the high acute toxicity (oral, dermal and inhalation) of the compound. Even though, depending of the exposure this might still be a reason of concern. The panel stated that it is in principle possible to identify a threshold. Nevertheless, as no robust long term and oncogenicity study is available in the dossier and no reliable long term NOAEL can be set, the data requirement, regarding a long term study, proposed by the rapporteur Member State originally in the DAR is confirmed. This implies that it is still not possible to set the reference values since there is no full picture of the toxicological properties of the compound. Thus, the risk assessment is still to be considered as inconclusive.

2.1 ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

After oral exposure, at least 93% is absorbed. A substantial part of absorbed dichlorvos is retained in the tissues of the exposed animal (about 30% of the absorbed radioactivity). The excretion of about 70 % via urine is rapid. Within a few days, the excretion is virtually complete. Dichlorvos is removed from the blood within 15 minutes. No accumulation of dichlorvos is found after repeated exposure.

Two main biotransformation pathways can be distinguished: a pathway starting with hydrolysis and a pathway starting with demethylation, the former being much more important than the latter for most of the mammals investigated.

The metabolites are excreted via the exhaled air (carbon dioxide) and the urine (dimethyl phosphate, phosphate, dichloroethanol glucuronide, hippuric acid, mercapturic acid, methyl-cystein and urea).

A new metabolism study was presented in the addendum and the experts concluded that the findings were consistent with previous findings, and confirmed an oral absorption value of >80%.

The meeting considered metabolites of potential toxicological concern. Desmethyl dichlorvos, 2,2-dichloroacetaldehyde and 2,2-dichloroacetic acid were identified as soil/water residues. While they are all present *in vivo* in the rat and mouse, no toxicity data is available for them. Additionally, dichlorvos is classified as very toxic/toxic by acute exposure, and there are significant concerns in relation to its potential genotoxicity/carcinogenicity. Therefore the metabolites must be considered as toxicologically relevant.

2.2 ACUTE TOXICITY

Dichlorvos is toxic following acute oral and dermal exposure (LD_{50} 57 mg/ kg bw and 120 mg/kg bw, respectively). It is very toxic after acute inhalation exposure, (LC_{50} 0.083 mg/L).

Due to the high acute systemic toxicity of dichlorvos, its skin and eye irritating properties could not be properly evaluated. Based on the available results, however, it is expected that dichlorvos is slightly irritating to the skin and eyes. Dichlorvos was found to have a skin sensitizing potential in Guinea pigs. Concerns were raised by the experts in relation to the fact that classification for skin and eye irritancy could not be determined due to toxicity, particularly in the light of indications of irritancy in operators and human volunteer studies. The experts considered that the risk phrase **R24**

"Toxic in contact with skin" would be appropriate. However, the issue will be discussed at the ECB. The following classification was also proposed: **R25 "Toxic if swallowed", R26 "Very toxic by inhalation", R43 "May cause sensitization by skin contact"**.

Due to the high acute toxicity, an analytical method for blood is required according to the Directive 96/46/EC. However, as dichlorvos is rapidly metabolised it is inappropriate for use as a marker in poisoning incidents. A new data requirement was therefore set for the notifier to propose a method using a non transient analyte that can be used specifically with blood samples in poisoning circumstances.

2.3 SHORT TERM TOXICITY

Based on results from the 13 week gavage study in rats, the NOAEL is 0.1 mg/kg/day. In the 52 week oral study in dog, the NOAEL is 0.05 mg/kg/day, based on significant decreases in the plasma, erythrocyte, and/or brain (males only) cholinesterase levels at 1.0 mg/kg/day (presented in the Addendum). Although studies were considered to be of low quality, proposed NOAELs were agreed with by the experts.

2.4 GENOTOXICITY

The experts discussed the information pertaining to the genotoxic potential of dichlorvos presented in the DAR and the statement of the UK Committee on Mutagenicity (2002). It was noted that many of the studies evaluated by the UK Committee on Mutagenicity had methodological deficiencies, and therefore could not be used to either confirm or exclude mutagenicity. In relation to the COMET assay in mouse keratinocytes after topical application, it was noted that while a positive result was obtained, it was a non routine study not widely used and not properly validated. In relation to the numerical chromosomal aberrations in rat bone marrow, it was noted that methodological deficiencies hampered the evaluation of results. In relation to the gene mutation assay in transgenic mice, it was noted that the dose levels used were sufficient to cause mortality. The mechanism of genotoxicity was considered to be methylation-mediated, but, as concluded in the JMPR evaluation, experts considered that the rate of methylation was nine orders of magnitude greater than that of phosphorylation, so that mutagenic activity should only be apparent at doses at which significant cholinergic symptoms effects were apparent.

The classification of dichlorvos as a contact mutagen by the UK Committee on Mutagenicity review was discussed. It was noted that dichlorvos is rapidly metabolised after oral administration, and that systemic exposure is limited: this is consistent with observations that genotoxicity is more pronounced in the absence of exogenous metabolic activation, and that dichlorvos is not mutagenic in systemic *in vivo* assays. The relevance of local effects to operators was discussed in the context of proposed uses, and it was considered that risk of inhalation and dermal exposure was limited. Additionally, the mutagenicity of dichloroacetaldehyde was considered. While it is mutagenic, the rate of production was such that relatively high doses, near the LD_{50}, were needed before significant levels were present.

As no final agreement could be reached, the experts concluded that a question addressing the mutagenic and carcinogenic potential of dichlorvos should be forwarded to the EFSA PPR panel.

EFSA notes: The opinion is summarised in the introductory part of chapter 2. It is concluded that it is an *in vitro* mutagen and that there are limited evidence that it is an *in vivo* contact mutagen. It was noted that although several of the studies show methodological deficiencies there are evidence that dichlorvos is a weak DNA alkylating agent. Thus, the issue of the mutagenic potential remains still not completely clear.

2.5 LONG TERM TOXICITY

EPCO experts considered the range of 11 cancer bioassays, of which 2 were equivocal/positive. The evidence of increased leukaemia in mice was noted; however this was of questionable significance due to the absence of a clear dose response. The evidence of increased adenomas in rats was noted, but, the significance of the increase in incidence in treated animals was questionable, as incidence was high in controls

Experts questioned whether these cancer bioassays, were sufficient to provide a weight of evidence assessment, and that it would be anticipated that 11 studies would be adequate to detect a dose-related increase in cancer incidence. However the quality and power of a number of studies was relatively low. The experts considered that while there was no consistent evidence of carcinogenicity, data was not adequate to exclude carcinogenic activity.

The experts agreed to set a tentative NOAEL based on the 2-year dog which that is 0.008 mg/kg bw/day based on the effects on cholinesterase activity at 0.08 mg/kg bw/day.

The applicability of R40 was discussed. However, it was felt appropriate to await the ECB decision on this classification. The question is also formulated to the EFSA PPR panel.

EFSA notes: The PPR opinion is available and is summarised in the introductory part of chapter 2. In relation to the conclusion drawn by the Panel EFSA confirms the data requirement for a combined long term and oncogenicity study to be submitted. Furthermore, it should be noted that NOAEL is tentative NOAEL and is based on a supplemental study which is not according to any guideline, not GLP and the results available are limited (Jolley, 1967). Generally, the use of a 2-year dog study is only applicable if it can be compared to results from rat and/or mouse long term studies.

2.6 REPRODUCTIVE TOXICITY

Reproductive toxicity

The NOAEL for maternal toxicity was 0.5 mg/kg bw/day. Only minor reductions in plasma and erythrocyte cholinesterase levels were observed at this dose, with no statistically significant inhibition of brain cholinesterase. The NOAEL for reproductive and offspring toxicity was 2 mg/kg bw/day.

Developmental toxicity

The developmental toxicity studies available in the DAR for the evaluation of dichlorvos do not meet the most recent guidelines for developmental toxicity. The experts discussed the study presented in the addendum, and confirmed the NOAEL of 0.5 mg/kg bw based on reduction of cholinesterase activity.

2.7 NEUROTOXICITY

Based on the available data, no delayed neuropathy was observed.

The experts expressed some concerns relating to changes in acetylcholine levels since cholinesterase inhibition may affect the development of the nervous system. However, it was considered that increased sensitivity of offspring to cholinesterase inhibition was not demonstrated in the multigeneration study, and that while dichlorvos inhibits NTE (neurotoxic esterase), this occurs at very high doses (ten times the LD_{50}). The experts therefore concluded that additional studies were not required.

2.8 FURTHER STUDIES

Human studies

There is extensive information available on the effects of dichlorvos in humans. A number of case studies showed dichlorvos to cause irritation and dermatitis upon dermal contact. Most studies, however, reflect the effects on the activity of plasma cholinesterase and/or erythrocyte acetyl cholinesterase. The evaluation of a series of studies in which humans were exposed to known concentrations of dichlorvos results in a respiratory threshold limit value of 0.1 mg/m^3 (time-weighted average 24 h) for the general population. For an adult of 70 kg, breathing 20 m^3 per 24 h, this concentration can be converted in a dose of 2 mg/d or 0.03 mg/kg bw/day. The results of various volunteer studies confirm these values. The human studies submitted were evaluated and considered inappropriate for derivation of reference values; however, they were considered by the experts for use as supportive data. It was noted that limited information on ethics was available.

Impurity

The rapporteur Member State indicated that chloral was a toxicologically relevant impurity and it has still to be proven that the batches used in the toxicological studies cover the proposed maximum limit of 5 g/kg.

2.9 MEDICAL DATA

The value of epidemiological data in the assessment of dichlorvos carcinogenicity was discussed. It was concluded that the value of data from workers was confounded by exposures to multiple pesticides. It was noted that studies with household insecticides often indicated an increased risk (e.g. leukaemia). However, while dichlorvos was often mentioned, the nature of insecticides was not determined. In over 500 studies, 15 were positive (arsenic compounds), while the remainder were inconclusive.

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

The tentative reference values proposed by the rapporteur Member State were discussed at the experts' meeting. The experts discussed the derivation of reference values in light of the proposed question relating to mutagenicity and carcinogenicity to be forwarded to the EFSA PPR panel. The

experts considered that mutagenicity data was inconclusive and a threshold had not been adequately identified. Therefore information and expertise was considered insufficient for the setting of reference values.

The EPCO agreed on the following tentative values, awaiting the opinion of the PPR panel. Based on the incomplete data package, the *tentative ADI is 0.00008 mg/kg bw/day* from the 2-year dog study, the *tentative AOEL is 0.0005 mg/kg bw/day* from the 1-year dog study and the *tentative ARfD is 0.002 mg/kg bw* from the rat teratogenicity study, with the safety factor of 100 applied.

EFSA notes: Based on the available opinion of the PPR Panel, as there are still uncertainties and data requirement identified (see chapter 2), neither the reference values nor or the safety factor(s) are possible to be confirmed in the light of uncertainties on the overall picture of the toxicological properties and the data requirement for a long term study.

2.11 DERMAL ABSORPTION

A dermal absorption of 30% was agreed on for the risk assessment for both diluted and concentrated dichlorvos.

2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The operator exposure risk assessment is dependant on the derivation of the reference values, and accordingly was not considered appropriate until the outcome of the EFSA PPR panel discussions on the genotoxicity and carcinogenicity of dichlorvos.
EFSA notes: the AOEL is not confirmed; see 2, 2.3, 2.4, 2.5 and 2.10.

The estimated operator worker and bystander exposure were discussed during the experts´ meeting and it was concluded that no significant worker or bystander exposure is anticipated. However, the meeting concluded that the information in the DAR on the operator exposure were not sufficient to conclude on the exposure and further clarifications were needed. New data were provided by the applicant in October 2005, which are neither peer reviewed nor presented in an addendum.

As the proposed application method is automatic (room treatment of bulbs), the primary concern identified related to **re-entry**. However, this would occur a number of hours after application, thus no significant exposure is anticipated. The meeting considered that the issue should be addressed at a Member State level, permitting account to be taken of the specific details of the applications and potential exposures.
EFSA note: In conclusion, the operator risk assessment is inconclusive based on the fact that the estimated exposure has weakness and the lack of an agreed AOEL.

No **bystander** exposure was anticipated. However, the issue will be addressed at a Member State level, permitting account to be taken of the specific details of the applications and potential exposures.

3. Residues

Dichlorvos was discussed in the experts' meeting for residues in June/July 2005 (EPCO 29)

In course of the evaluation procedure the notifier has submitted a new table of representative uses supporting only treatment of flower-bulbs, which are not food and feed commodities. The evaluation of the residue behaviour of dichlorvos in plant and animals and a dietary risk assessment for consumers is not relevant for that use.
However, in an earlier attempt to define representative uses for the evaluation procedure related to Annex I inclusion of dichlorvos a use on stored cereals was intended and therefore assessed in the DAR. The rapporteur Member State noted that the documentation provided by the applicant is absolutely insufficient to provide reliable information about the residue behaviour of dichlorvos applied to cereals stored in silos or warehouses. From the mainly as published articles submitted data it is impossible to assess the validity of the presented results. In addition, the few studies provided are from the early 1970's and do not specify necessary information about e.g. sampling methods and storage conditions before analysis.

The experts' meeting for residues considered the residues data insufficient for uses with relevance for consumer exposure and confirmed the rapporteur Member State proposal that a full residue data package in accordance to the requirements of directive 91/414/EEC will be required to support such uses, if MS authorisation is sought.

4. Environmental fate and behaviour

Dichlorvos was discussed at the EPCO experts' meeting for environmental fate and behaviour (EPCO 26) in June 2005 on the basis of addendum 1 to the DAR dated May 2005.

4.1. FATE AND BEHAVIOUR IN SOIL

For the representative use to treat flower bulbs post harvest in store, exposure of the soil environmental compartment is excluded. Information on the fate and behaviour of dichlorvos in soil is therefore not required to complete the risk assessment. Whilst some data were available and were summarised in the original DAR, these data have not been peer reviewed by the experts from member states or the EFSA.

4.2. FATE AND BEHAVIOUR IN WATER

When appropriate horticultural practice is followed, flower bulbs are washed before treatment with dichlorvos. Therefore unlike post harvest storage treatments of other plant products, contamination of surface water with bulb wash water will not occur. Therefore for the representative use to treat flower bulbs post harvest in store, exposure of the natural surface water environmental compartment is

excluded. Information on the fate and behaviour of dichlorvos in natural water systems is therefore not required to complete the risk assessment. Whilst some data on the fate and behaviour of dichlorvos in sediment water systems were available and were summarised in the original draft assessment report, these data have not been peer reviewed by the experts from member states or the EFSA.

In an acceptable OECD guideline ready biodegradability study[5] that utilised a sewage sludge innoculum, dichlorvos was classified as 'readily biodegradable' based on a test concentration of 2mg/L but 'not readily biodegradable' based on a test concentration of 5mg/L. Member state experts considered that as a result of this study, for classification purposes dichlorvos should be considered 'not readily biodegradable'.

4.3. FATE AND BEHAVIOUR IN AIR

Based on its vapour pressure (2.1 Pa at 25°C), dichlorvos (a liquid) is classified as volatile. Based on its Henry's Law constant (2.58×10^{-2} Pa. m^3. mol^{-1}, resulting in a dimensionless Henry's Law air water partition coefficient of 1.06×10^{-5} at 20°C) it is classified as moderately volatile from aqueous systems. Therefore from the representative indoor use, exposure of air may occur when stores are vented after treatment. However wet and dry re-deposition to land and surface waters would be expected to be negligible. Dichlorvos would not be expected to be subject to long range transport in the upper atmosphere, as using the method of Atkinson and the Atmospheric Oxidation Program (v.1.86) to estimate photochemical reaction with hydroxyl radicals, rate constants of 6.381×10^{-12} to 9.4×10^{-12} cm^3 $molecule^{-1}sec^{-1}$ were estimated. Assuming an atmospheric concentration of 1.5×10^6 hydroxyl radicals cm^{-3} an atmospheric half life of 13-20 hours was calculated.

5. Ecotoxicology

Dichlorvos was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 27) in June 2005.

5.1. RISK TO TERRESTRIAL VERTEBRATES

All acute and dietary toxicity studies submitted for birds were assessed by the rapporteur Member State as not acceptable except the dietary toxicity study of Hill & Camardese (1986). No study on the reproduction toxicity to birds was submitted. The EPCO experts concluded that also the study of Hill & Camardese (1986) is not acceptable but that exposure of birds and mammals from the representative indoor use in flower bulbs is unlikely and therefore no further studies are required to address the risk to birds.

5.2. RISK TO AQUATIC ORGANISMS

Nine studies on the acute toxicity and seven studies on the chronic toxicity to fish were submitted but all of them were assessed as not acceptable. No analytical verification of the test concentrations was

[5] See addendum to the DAR dated May 2005.

performed in the studies with daphnids and in the studies with algae. Therefore a data requirement was set in the evaluation meeting of March 2005 to submit valid studies with *Daphnia magna* and algae. Two acute toxicity studies with fish were made available by the applicant and summarized in the addendum of Mai 2005 but no new studies with daphnids and algae were submitted. It was agreed in the EPCO meeting that the studies are required for classification and labelling but are not necessary for the risk assessment for the indoor use in flower bulbs assuming that exposure of surface water is negligible.

5.3. RISK TO BEES

The EPCO meeting agreed that no risk assessment is needed for the indoor use because bees are not expected to be exposed.

5.4. RISK TO OTHER ARTHROPOD SPECIES

The studies with non-target arthropods were assessed as not valid. The EPCO meeting agreed that a risk assessment is not needed for the indoor use on flower bulbs because non-target arthropods are not expected to be exposed to dichlorvos.

5.5. RISK TO EARTHWORMS

The available study on the acute toxicity to earthworms was assessed as not valid. The EPCO meeting decided that a risk assessment is not needed for the indoor use because earthworms are not expected to be exposed.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

No exposure of other soil non-target organisms is expected from the indoor use on flower bulbs.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No exposure of soil non-target micro-organisms is expected from the indoor use on flower bulbs.

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

No exposure of other non-target organisms is expected from the indoor use on flower bulbs.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The potential risk to sewage treatment plants from the indoor use on flower bulbs is considered to be low. No inhibitory effects on the respiration of sewage sludge was observed at the tested dose of 100 mg a.s./L.

6. Residue definitions

Soil

Definitions for risk assessment: not required for representative use

Definitions for monitoring in the case of accident or misuse: dichlorvos

Water

Ground water

Definitions for exposure assessment: not required for representative use

Definitions for monitoring in the case of accident or misuse: dichlorvos

Surface water

Definitions for risk assessment: not required for representative use

Definitions for monitoring in the case of accident or misuse: dichlorvos

Air

Definitions for risk assessment: dichlorvos

Definitions for monitoring: dichlorvos

Food of plant origin

Definitions for risk assessment: not required for representative use

Definitions for monitoring: not required for representative use

Food of animal origin

Definitions for risk assessment: not required for representative use

Definitions for monitoring: not required for representative use

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

Soil

Assessed pattern of use precludes soil exposure.

Ground water

Assessed pattern of use precludes groundwater exposure.

Surface water and sediment

Assessed pattern of use precludes exposure of natural surface water systems.

Air

Compound (name and/or code)	**Toxicology**
dichlorvos	Very toxic via inhalation (LC_{50} 0.083 mg/L). T^{+}; R26 classification proposed. No study on repeated exposure.

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

- Clarification with respect to the proposed minimum purity of dichlorvos and the proposed maximum levels for the impurities in the technical material (date of submission unknown, data gap identified by the meeting of experts, refer to chapter 1). Depending on this further data with respect to the analytical methods could be required.
- Spectra (UV data) for dichlorvos (study submitted to the rapporteur Member State in September 2005, but neither peer reviewed by MS not discussed in a meeting of experts; refer to chapter 1).
- Spectra for the relevant impurity chloral according to Directive 94/37/EC (date of submission unknown, data gap identified in the DAR and confirmed by the meeting of experts; refer to chapter 1).
- A shelf-life study to demonstrate that the relevant impurity chloral in the technical material is not increasing in the formulation upon storage. (date of submission unknown, data gap identified by EFSA after the meeting of experts, taken the response from the rapporteur Member State in the evaluation table into account, refer to chapter 1).
- A study for the hydrolysis of dichlorvos (study submitted to the rapporteur Member State in September 2005,but neither peer reviewed by MS not discussed in a meeting of experts; refer to chapter 1)
- Information on one certain formulant in the representative formulation (date of submission unknown, data gap identified at the evaluation meeting and confirmed by the meeting of experts, refer to chapter 1).
- Data on the pH value of the representative formulation (study submitted to the rapporteur Member State in September 2005, refer to chapter 1).
- Analytical method for the determination of residues in soil (study announced by the notifier for June 2005, but the rapporteur Member State has not received a study yet, data gap identified at the evaluation meeting and confirmed by the meeting of experts; refer to chapter 1).
- Analytical method for the determination of residues in water (study announced by the notifier for June 2005, but the rapporteur Member State has not received a study yet, data gap identified at the evaluation meeting and confirmed by the meeting of experts; refer to chapter 1).
- Analytical method for the determination of residues in air (study available, April 2006, but neither peer reviewed nor discussed in a meeting of experts, data gap identified at the evaluation meeting and confirmed by the meeting of experts; refer to chapter 1).
- An analytical method for the determination of residues of dichlorvos in blood and animal tissues to cover the requirement of Directive 96/46/EC for substance classified as very toxic (Annex point 4.2.5) (date of submission unknown, data requirement identified in the DAR and confirmed by the meeting of experts; refer to chapter 1 and 2.2).
- The need for a repeated inhalation study was identified in the DAR and confirmed at the experts meeting (refer to chapter 2.3).

- Combined long term and oncogenicity study to be submitted, data requirement was identified in the DAR and confirmed after the experts meting and the adoption of the PPR opinion (see chapter 2).
- New studies with daphnids and algae (not relevant for the risk assessment for the representative use in flower bulbs but needed for classification and labelling; data requirement identified at the evaluation meeting in March 2005; no submission date proposed; see chapter 5.2).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide comprise room treatment (by using fogging vaporising equipment) to protect flower bulbs from thrips. The application rate is 2.2 g dichlorvos per 100 m³ with maximal 3 applications resulting in a maximum total dose of 6.6 g/100 m³. Dichlorvos can be used as acaricide and insecticide. It should be noted that the applicant stated that only the use as insecticide will be supported in the EU review programme.

The representative formulated product for the evaluation was "Dichlorvos 550 g/L EC", an emulsifiable concentrate (EC), registered in some Member States of the EU.

No methods are available to monitor the compounds given in the respective residue definition for soil water and air.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that at least limited quality control measurements of the plant protection product are possible.

Dichlorvos is toxic following acute oral and dermal exposure and very toxic after acute inhalation exposure. It is expected to be slightly irritating to the skin and eyes. Dichlorvos was found to have a skin sensitizing potential. The following classification was proposed: **R25 Toxic if swallowed, R24 Toxic in contact with skin, R26 Very toxic by inhalation, R43 May cause sensitization by skin contact.** Dichlorvos did not pose any concern for reproductive and developmental toxicity. Based on the available data, no delayed neuropathy was observed. A question addressing the mutagenic and carcinogenic potential of dichlorvos was proposed to be forwarded to the EFSA PPR panel due to the weaknesses of data provided, not adequate to exclude carcinogenic activity. Therefore the derivation of the reference doses including safety factor, and accordingly the operator exposure calculations, was not considered appropriate until the outcome of the EFSA PPR panel discussions. The PPR opinion has been adopted on 1 April 2006. Taking the conclusions in the opinion into consideration it was agreed at the meeting with Member State's representatives in April 2006 that the risk assessment is still inconclusive due to the uncertainties of the genotoxic and carcinogenic properties of dichlorvos also considering the overall poor quality of the dossier.

The evaluation of the residue behaviour of dichlorvos in plants and livestock animals and a dietary risk assessment for consumers is not relevant for the representative use.
It is noted that residues data are insufficient for uses with relevance for consumer exposure and a full residue data package in accordance to the requirements of directive 91/414/EEC would be necessary to support such uses.

For the applied for representative use it has been concluded that information on the fate and behaviour of dichlorvos is soil, surface water and groundwater is not required to complete the environmental exposure assessment. The available data on fate and behaviour in air are considered sufficient to characterise the expected behaviour in this environmental compartment.

The risk to birds and mammals, aquatic organisms, bees, other non-target arthropods, earthworms and other non target organisms, soil non-target micro-organisms was considered as low because exposure is assumed to be negligible for the representative indoor use in flower bulbs. The risk posed to biological methods of sewage treatment was assessed as low.

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

- None.

Critical areas of concern

- At the moment it is not possible to define a technical specification for dichlorvos.
- There is only one and very restricted use, as indoor flower bulb treatment.
- Due to poor data package, genotoxicity and carcinogenicity cannot be concluded. Questions were forwarded to the EFSA PPR Panel. The PPR opinion has been adopted 1 April 2006 (for full reference see footnote page 2). Taking the conclusions in the opinion into consideration it was agreed at the Working group Evaluation Meeting in April 2006 that the risk assessment is still inconclusive due to the uncertainties of the genotoxic and carcinogenic properties of dichlorvos also considering the overall poor quality of the dossier. The data requirement for a combined long term and oncogenicity study to be submitted is confirmed.
- No definitive reference values are confirmed.
- As definitive reference values were not agreed on, risk assessment to operators, workers and bystander is considered as inconclusive.
- No enforcement methods for soil, water, air as well as animal tissues and blood are available.

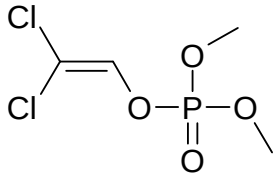
APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

(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) ‡	Dichlorvos, synonyms: Denkavepon, Vapona, Nuvan, Nogos, DDVP
Function (e.g. fungicide)	Insecticide, acaricide
Rapporteur Member State	Italy
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	2,2-dichlorovinyl dimethyl phosphate
Chemical name (CA) ‡	Phosphoric acid, 2,2-dichloroethenyl dimethyl ester
CIPAC No ‡	11
CAS No ‡	62-73-7
EEC No (EINECS or ELINCS) ‡	200-547-7
FAO Specification ‡ (including year of publication)	CODE AGP: CP/239 year 1989 Impurities: Chloral: max 5g/kg Water: max 0.5g/kg
Minimum purity of the active substance as manufactured ‡ (g/kg)	The minimum purity of the active substance as manufactured is 950 g/kg ***(open point)***
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	Chloral (trichloroacetaldehyde): 5 g/kg
Molecular formula ‡	$C_4H_7Cl_2O_4P$
Molecular mass ‡	221.0
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) ‡	Not applicable is liquid (< -80 °C freezing point) (>98% purity)
Boiling point (state purity) ‡	Boiling not observed, under test condition ,(atmospheric pressure of 101.325 kPa, method EEC A2, 1992) Decomposes at test conditions (98% purity)
Temperature of decomposition	>190°C (98% purity)
Appearance (state purity) ‡	very pale yellow clear liquid
Relative density (state purity) ‡	Density = 1.42 kg/L at ca. 20 °C (98% purity)
Surface tension	63.5 mN/m at 20 °C (1.012 g/L)
Vapour pressure (in Pa, state temperature) ‡	2.1 Pa at 25 °C (99.8% purity)
Henry's law constant (Pa m^3 mol^{-1}) ‡	2.58 x 10^{-2} Pa. m^3/mol at 25 °C
Solubility in water ‡ (g/l or mg/l, state temperature)	18 g/L at 25 °C The test substance does not dissociate or associate between in the pH range 5 to 9 so the water solubility is not pH dependent (99.8% purity)
Solubility in organic solvents ‡ (in g/l or mg/l, state temperature)	At 25 °C dichlorvos is completely miscible with: ethanol, acetone, toluene, *n*-octanol and *n*-hexane (concentrations ranged from 5 to 95% v/v) Dichlorvos is soluble with 1,2-dichloethane, ethyl acetate at ratio 1:1. Both mixtures were clear single liquid media.
Partition co-efficient (log POW) ‡ (state pH and temperature)	log Kow = 1.9 (± 0.11) at 25 °C (99.8% purity)
Hydrolytic stability (DT50) ‡ (state pH and temperature)	*Data required*
Dissociation constant ‡	From molecular structure dichlorvos seems not have acid/basic dissociation
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	*The given data are neither peer reviewed nor presented in the DAR or a respective addendum.* UVmax = 204 nm ε < 10 M^{-1} cm^{-1} at wavelengths > 290 nm
Photostability (DT50) ‡ (aqueous, sunlight, state pH)	Not required since the molar absorption coefficient (ε) < 10 M^{-1} cm^{-1} at wavelengths > 290 nm
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	Not applicable because the phototransformation of dichlorvos in water is negligible
Flammability ‡	*Data/clarification required*
Explosive properties ‡	*Data/clarification required*

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

List of representative uses evaluated*

Crop and/or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
(a)			(b)	(c)	Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water L/ha min max	kg as/ha min max	(l)	(m)
Flower-bulbs	EU	Dichlorvos 550 g/L EC	I	Thrips	EC	550 g/L	Room treatment	N.A.	Max: 3	2 days	2.2 kg/hL	45 L/ha	2.2 g/100 m^3	N.A.	Application rate based on an average height of 4.5 m for a storage [1]
Starting material of strawberries, eggplants, cucumber, paprika, red pepper, tomatoes and other crops	EU	Dichlorvos 550 g/L EC	G	Aphid, thrips, white fly	EC	550 g/L	Room treatment	Starting material	Max.: 3	2 days	2.2 kg/hL	45 L/ha	0.99 kg/ha	N.A.	[2]
Flowering crops	EU	Dichlorvos 550 g/L EC	G	Aphid, thrips, white fly	EC	550 g/L	Room treatment	All stages	Max.: 3	2 days	2.2 kg/hL	45 L/ha	0.99 kg/ha	N.A.	[2]
Ornamental plants and trees	EU	Dichlorvos 550 g/L EC	G	Aphid, thrips, white fly	EC	550 g/L	Room treatment	All stages	Max.: 3	2 days	2.2 kg/hL	45 L/ha	0.99 kg/ha	N.A.	[2]

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

Appendix 1 – list of endpoints

Crop and/or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
(a)			(b)	(c)	Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water L/ha min max	kg as/ha min max	(l)	(m)
Cereals in store	EU	Dichlorvos 550 g/L EC	I	Insects (Beetles, weevils etc.)	EC	550 g/L	Room treatment	N.A.	Max.: 1	N.A.	N.A.	N.A.	7.5 g/100 m^3		[2]
Cereals in silos	EU	Dichlorvos 550 g/L EC	I	Insects (Beetles, weevils etc.)	EC	550 g/L	N.A.	N.A.	Max.: 1	N.A.	N.A.	N.A.	7 g/t		[2]

[1] The risk assessment for operator, worker and bystander is inconclusive, see section 2.

[2] The risk assessment was not completed since the applicant does not support this use for the review at EU level.

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)	Dichlorvos as technical product can be determined according to accepted analytical methods. A generally accepted method is the product analysis by reaction with excess of iodine that is estimated by titration: This method is described in CIPAC Handbook, 1980, 1A, 1214. Another method is gas chromatography (GLC), which is described in "CIPAC Proceedings", 1981, 3, 173. Procedures are described for the analysis of dichlorvos technical by infrared spectroscopy and by an iodometric method: IR or GC/FID (method AW.1/5 GC/FID
Impurities in technical as (principle of method)	No validated data
Plant protection product (principle of method)	See technical product

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	*Not applicable since not residue definition is proposed.*
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	*Not applicable since not residue definition is proposed.*
Soil (principle of method and LOQ)	*Method required*
Water (principle of method and LOQ)	*Method required*
Air (principle of method and LOQ)	*Method required*
Body fluids and tissues (principle of method and LOQ)	*Data required*, since dichlorvos metabolise rapidly and extensively

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	Not classified

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

Appendix 1.3: Impact on Human and Animal Health

Note: the overall quality of the database is not to current standards.

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

Rate and extent of absorption ‡	Rapid, >80% based on urine excretion
Distribution ‡	Residual carcass (13% to 26%), liver (3% to 5%), and all other tissue combined (1% to 2%).
Potential for accumulation ‡	Not assessable due to incorporation into bio molecules
Rate and extent of excretion ‡	Expired air (40% to 58%), urine (11% to 17%), and faeces (4% to 7%). The majority of the radioactivity in expired air and excreta was eliminated within 24 hours after dosing.
Metabolism in animals ‡	Extensive by hydrolysis and demethylation
Toxicologically significant compounds ‡ (animals, plants and environment)	Dichlorvos. The metabolites desmethyl dichlorvos, 2,2-dichloroacetldehyde and 2,2-dichloroacetic acid are considered as toxicologically relevant. The impurity chloral is considered as toxicologically relevant, but no data is available.

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	80 mg/kg bw	**R25**
Rat LD_{50} dermal ‡	120 mg/kg bw	**R24**
Rat LC_{50} inhalation ‡	0.083 mg/L	**R26**
Skin irritation ‡	Not assessed due to high toxicity	
Eye irritation ‡	Not assessed due to high toxicity	
Skin sensitization ‡ (test method used and result)	Skin sensitiser (Split Adjuvant Test)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Nervous system / Cholinesterase inhibition
Lowest relevant oral NOAEL / NOEL ‡	0.5 mg/kg/day , 52 wks oral study, dog
Lowest relevant dermal NOAEL / NOEL ‡	No good studies available
Lowest relevant inhalation NOAEL / NOEL ‡	No study – *Data gap*

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

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	Positive *in vitro*. Inconclusive in vivo. Referred to EFSA-PPR panel

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

Target/critical effect ‡	Cholinesterase inhibition
Lowest relevant NOAEL / NOEL ‡	***Tentative value****: NOAEL 0.008 mg/kg (LOAEL 0.08 mg/kg), 2 year oral study, dog
Carcinogenicity ‡	Inconclusive. (Positive 2 out of 11 studies evidence of pancreatic adenomas and leukemia) Quality of studies generally low. Referred to EFSA-PPR Panel.

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Parental and pups ChE inhibition, decreased body weight, reduced pup survival
Lowest relevant reproductive NOAEL / NOEL ‡	Maternal 0.5 mg/kg/day Reproductive/offspring toxicity 2 mg/kg/day
Developmental target / critical effect ‡	No evidence. Studies not to current standards
Lowest relevant developmental NOAEL / NOEL ‡	Oral rabbit: Developmental 5 mg/kg bw/day (rabbit, highest dose tested) Maternal: No NOAEL can be derived Inhalation: Developmental: > 6.25 µg/L (ca 1.7 mg/kg bw/day (rat and rabbit, highest dose) Maternal 0.25 µg/L

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

.....	No potential for delayed neuropathy (rat)

Other toxicological studies ‡ (Annex IIA, point 5.8)

.....	Alterations of liver enzyme activities at doses higher than the ones causing ChE inhibition, neurobehavioral effects.

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

Medical data ‡ (Annex IIA, point 5.9)

.....	A number of case studies showed dichlorvos to cause irritation and dermatitis upon dermal contact. Most studies, however, deal with the effects on the activity of plasma cholinesterase and/or erythrocyte acetyl cholinesterase.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	Information was considered insufficient for the setting of reference values.		
AOEL ‡	Information was considered insufficient for the setting of reference values.		
ARfD ‡ (acute reference dose)	Information was considered insufficient for the setting of reference values.		

Dermal absorption (Annex IIIA, point 7.3)

.....	30% concentrated and diluted product *based on in vivo* rat data

Acceptable exposure scenarios (including method of calculation)

Operator	Inconclusive
Workers	Inconclusive
Bystanders	Inconclusive

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	T+;	Very toxic,
	R24	Toxic in contact with skin
	R25	Toxic if swallowed
	R26	Very toxic by inhalation
	R43	May cause sensitisation by skin contact
	(R40	Limited evidence of carcinogenic effect. Due to inconclusive nature of mutagenicity and carcinogenicity, the applicability of R40 has not been determined)

‡ 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	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Rotational crops	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Plant residue definition for monitoring	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Plant residue definition for risk assessment	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Conversion factor (monitoring to risk assessment)	Documentation provided on the residue behaviour is not sufficient for edible crop uses

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

Animals covered	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Animal residue definition for monitoring	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Animal residue definition for risk assessment	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Conversion factor (monitoring to risk assessment)	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Metabolism in rat and ruminant similar (yes/no)	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Fat soluble residue: (yes/no)	Documentation provided on the residue behaviour is not sufficient for edible crop uses

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

.....	Documentation provided on the residue behaviour is not sufficient for edible crop uses

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

.....	Documentation provided on the residue behaviour is not sufficient for edible crop uses

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

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: yes/no	Poultry: yes/no	Pig: yes/no
Muscle Liver Kidney Fat Milk Eggs	Documentation provided on the residue behaviour is not sufficient for edible crop uses		

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

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

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL	STMR (b)
Documentation provided on the residue behaviour is not sufficient for edible crop uses					

* Not relevant for representative use on flower bulbs in storage
(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the critical GAP

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

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

ADI	Documentation provided on the residue behaviour is not sufficient for edible crop uses
TMDI (European Diet) (% ADI)	Documentation provided on the residue behaviour is not sufficient for edible crop uses
NEDI (% ADI)	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Factors included in NEDI	Documentation provided on the residue behaviour is not sufficient for edible crop uses
ARfD	Documentation provided on the residue behaviour is not sufficient for edible crop uses
Acute exposure (% ARfD)	Documentation provided on the residue behaviour is not sufficient for edible crop uses

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Documentation provided on the residue behaviour is not sufficient for edible crop uses			

* 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)

.....	Documentation provided on the residue behaviour is not sufficient for edible crop uses

* Not relevant for representative use on flower bulbs in storage

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

Appendix 1.5: Fate and Behaviour in the Environment

Note: The supported uses are only room treatment on flower-bulbs. These supported uses are of no concern for the environment.

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

Mineralization after 100 days ‡	Not relevant
Non-extractable residues after 100 days ‡	Not relevant
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	Not relevant

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

Anaerobic degradation ‡	Not relevant due to supported uses
Soil photolysis ‡	Not relevant due to supported uses

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

Method of calculation	Not relevant due to supported uses
Laboratory studies ‡ (range or median, with n value, with r^2 value)	Not relevant due to supported uses
	degradation in the saturated zone ‡: Not relevant due to supported uses
Field studies ‡ (state location, range or median with n value)	Not relevant due to supported uses
Soil accumulation and plateau concentration ‡	Not relevant due to supported uses

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	Not relevant due to supported uses

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

Column leaching ‡	Not relevant due to supported uses
Aged residues leaching ‡	Not relevant due to supported uses
Lysimeter/ field leaching studies ‡	Not relevant due to supported uses

‡ 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	Not relevant due to supported uses
Application rate	Not relevant due to supported uses

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)	Not relevant due to supported uses
Photolytic degradation of active substance and relevant metabolites ‡	Not relevant due to supported uses
Readily biodegradable (yes/no)	No
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡ - DT_{50} whole system ‡ - DT_{90} whole system ‡	Not relevant due to supported uses
Mineralization	Not relevant due to supported uses
Non-extractable residues	Not relevant due to supported uses
Distribution in water / sediment systems (active substance) ‡	Not relevant due to supported uses
Distribution in water / sediment systems (metabolites) ‡	Not relevant due to supported uses

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

Parent

Method of calculation	Not relevant due to supported uses
Application rate	Not relevant due to supported uses
Main routes of entry	Not relevant due to supported uses

PEC (sediment)

Parent

Method of calculation	Not relevant due to supported uses
Application rate	Not relevant due to supported uses

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

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Not relevant due to supported uses
Application rate	Not relevant due to supported uses

$PEC_{(gw)}$

Maximum concentration	Not relevant due to supported uses
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Not relevant due to supported uses

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

Direct photolysis in air ‡	Not studied, not required.
Quantum yield of direct phototransformation	Not applicable because the phototransformation of dichlorvos in water is negligible
Photochemical oxidative degradation in air ‡	The estimated half life (Atkinson method) of dichlorvos in the atmosphere (by hydroxyl radical oxidation) is 13 and 20 hours calculated with 1.5×10^6 OH-radicals/cm^3 and 12 hours day
Volatilization ‡	Data not available

PEC (air)

Method of calculation	Calculation not made

$PEC_{(a)}$

Maximum concentration	Considered low by expert judgement based on indoor use evaluated.

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	*Soil*: dichlorvos *Surface water*: dichlorvos *Groundwater*: dichlorvos *Air*: dichlorvos

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

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

Soil (indicate location and type of study)	-
Surface water (indicate location and type of study)	-
Ground water (indicate location and type of study)	-
Air (indicate location and type of study)	-

Classification and proposed labelling (Annex IIA, point 10)

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

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

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} 80 mg a.s./kg b.w. (oral rat)
Reproductive toxicity to mammals ‡	Not acceptable studies provided
Acute toxicity to birds ‡	Not acceptable studies provided but not necessary
Dietary toxicity to birds ‡	LC_{50} 251 ppm (Japanese quail)
Reproductive toxicity to birds ‡	Not necessary

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

As the use was flower bulbs in storage, no environmental concentration is foreseen. Therefore, TER for terrestrial vertebrates cannot be calculated.

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Laboratory tests ‡				
Oncorhynchus mykiss	Dichlorvos	96h	LC_{50}	0.55
Pimephales promelas	Dichlorvos	96h	LC_{50}	3.72
Fish	Dichlorvos	28d chronic	NOEC	Not acceptable studies provided but not necessary
Daphnia magna	Dichlorvos tech.	48h	EC_{50}	No acceptable studies available
Daphnia magna	Dichlorvos	21d chronic	NOEC	Not acceptable studies provided but not necessary
Selenastrum capricornutum	Dichlorvos tech.	94h	EC_{50}	No acceptable studies available
Chironomus riparius	Dichlorvos tech.	24h	EC_{50}	Not acceptable studies provided but not necessary

Microcosm or mesocosm tests
Not required

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

As the use was flower bulbs in storage, no environmental concentration is foreseen. Therefore, TER for aquatic organisms cannot be calculated.

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

Bioconcentration

Bioconcentration factor (BCF) ‡	Not requested: logPow = 1.9
Annex VI Trigger:for the bioconcentration factor	-
Clearance time (CT_{50}) (CT_{90})	-
Level of residues (%) in organisms after the 14 day depuration phase	-

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

Acute oral toxicity ‡	Not acceptable studies provided but not necessary
Acute contact toxicity ‡	Not acceptable studies provided but not necessary

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

As the use was flower bulbs in storage, no environmental concentration is foreseen. Therefore, TER for honey bees cannot be calculated.

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

Not acceptable studies provided but not necessary

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

Acute toxicity ‡	Not acceptable studies provided, but not necessary
Reproductive toxicity ‡	Not necessary

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

As the use was flower bulbs in storage, no environmental concentration is foreseen. Therefore, TER for earthworms cannot be calculated.

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

Nitrogen mineralization ‡	Dichlorvos has no effect on soil nitrification at concentrations up to 13.4 mg as/kg (a ten-fold of the field rate).
Carbon mineralization ‡	Dichlorvos has no effect on soil microbial biomass (measured by soil respiration) at concentrations up to 13.4 mg AS/kg (a ten-fold of the field rate).

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

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment

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

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

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

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