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Interim Chemical Review Committee
Fourth session
Rome, 3 – 7 March 2003
Item 5 a) i of the provisional agenda*

INCLUSION OF CHEMICALS IN THE INTERIM PRIOR INFORMED CONSENT PROCEDURE - SUPPORTING DOCUMENTATION

Parathion

Note from the Secretariat

1. Annexed to this note is the documentation provided by the European Community in support of their notification of final regulatory action on parathion.

* UNEP/FAO/PIC/ICRC.4/1

List of Documentation Annexed to UNEP/FAO/PIC/ICRC4/10/Add.2

Supporting documentation on Parathion from the European Commuinity:

- Full Report on Parathion, ECCO Peer Review Meetings, 2000
  The table of contents of the report and excerpt (page 1 to 48) are annexed to this note.
  The full report annexed to document UNEP/FAO/PIC/ICRC.4/10/Add.4 can be obtained from the Secretariat on request at the meeting.

- Monograph on the Review of Parathion, European Community
  Volume 1 of the monograph, which contains report and proposed decision, is annexed to this note.
  Volume 3 (330 + page) containing summary, scientific evaluation and assessment, is annexed to document UNEP/FAO/PIC/ICRC.4/10/Add.4 and can be obtained from the Secretariat on request at the meeting.

European Commission

Peer Review Programme

ECCO Peer Review Meetings

Full Report on
Parathion

- Reports of the meetings
- Comments on the draft assessment report
- Other documents considered at the meetings

ECCO-Team, at: Biologische Bundesanstalt für Land- und Forstwirtschaft, Braunschweig

30.11.2000

ECCO PEER REVIEW PROGRAMME

FULL REPORT ON **PARATHION**

CONTENTS

Specific comments from the **Overview Meeting** on the active substances are listed below. The conclusions of the meeting were as follows:

PARATHION

Rapporteur Member State: Italy

The following documents were tabled and discussed:

Date	Content	Supplier	ECCO Ref No.
undated	Updated list of end points (sections 1, 3, 4 and 5)	France	11123/ECCO/BBA/00
14 June 2000	Comment	Germany	11149/ECCO/BBA/00

1 Physical and chemical properties, Methods of analysis section

- No data requirements had been fulfilled. Twelve data requirements were classified as essential for unconditional Annex I inclusion. One new data requirement (1.13) was also considered essential for unconditional Annex I inclusion, see below. Three open points were considered fulfilled whereas one remains open (1.3).
- The new data requirement (1.13) existed already as 4.8 under the section mammalian toxicology but was moved to the methods of analysis section. This data requirement covers the answer to the message from ECCO 89 to ECCO 93 with regard to the question as to whether the LOQ for air is considered sufficiently low.
- The classification proposal for data requirement 1.6 was changed from 'MS' to 'A' because the information required on section B.3.5 is in any case essential for Annex I inclusion.
- Regarding data requirement 1.8, it was noted that it is considered still open because the residues have not been finally defined.
- Open point 1.3 remains open as a 'list of intended uses' has been submitted but a 'list of uses supported by available data' is still missing.
- The area of concern, very incomplete data set for Annex II and III, remains.

2 Environmental fate and behaviour section

- A discussion on environmental fate and behaviour did not take place at the ECCO 91-Peer Review Meeting. Just a list of six data requirements and three open points was compiled. The classification proposal for all data requirements was 'essential for unconditional Annex I inclusion'.
- It was pointed out that it looks as if these data requirements are all that is required for this section, and if these data was submitted, the section is complete. This is certainly not the case. The main data submitter has to submit a full data set. Therefore, the six data requirements were changed to one new requirement "Full Annex II and III data package for the fate and behaviour section is required" which is essential for unconditional Annex I inclusion.
- It was noted that the main data submitter did not make any comments on the whole section.
- Areas of concern were not discussed at the ECCO 91-Peer Review Meeting on fate and behaviour.

PARATHION (continued)

3 Ecotoxicology section

- No data requirement had been fulfilled. Eleven data requirements were either classified as essential for unconditional Annex I inclusion (3.1 – 3.8; 3.11) or considered to be dealt with at Member State level (3.9 and 3.10). Two new data requirements (3.12 and 3.13) were proposed which were classified as essential for unconditional Annex I inclusion, see below. Two open points were considered fulfilled whereas one remains open (3.3).
- The new data requirement (3.12) for which a risk assessment for birds under worst case conditions is required, resulted from open point 3.1.
- The new data requirement (3.13) for which a risk assessment for mammals under worst case conditions is required, resulted also from open point 3.1.
- The areas of concern, namely risk to birds, aquatic organisms, bees and other non-target arthropods, lack of information on the metabolites as well as incomplete risk assessments because of missing data on exposure, remain.

4 Mammalian toxicology section

- Three data requirements had been fulfilled. The four remaining data requirements were classified as essential for unconditional Annex I inclusion. One data requirement was moved to the physical and chemical properties section (4.8). One open points was considered fulfilled (4.2) whereas the other remains open (4.1).
- Regarding data requirement 4.5, it was stressed that it is not the ECCO 100 Overview Meeting which defines the intended uses (uses supported by available data) but the task and responsibility of the main data submitter to provide such a list.
- Although open point 4.2 was considered fulfilled it was noted that the list of end points still needs to be amended by replacing the 'list of intended uses' by the 'list of uses supported by available data'.
- The areas of concern, namely the fact that the AOEL is exceeded for operators, and the high risk of acute poisoning by all routes of exposure, remain.

5 Residues section

- One data requirement had been fulfilled. The six remaining data requirements were either classified as essential for unconditional Annex I inclusion (5.1 – 5.4; 5.7) or considered to be dealt with at Member State level (5.6). One open point was considered fulfilled (5.2) whereas the other remains open (5.1).
- The classification proposal for data requirements 5.3 and 5.4 was changed from 'MS' to 'A' because it was agreed that these data are essential for unconditional Annex I inclusion because insufficient data (e.g. no studies or old studies with data gaps) were submitted.
- Regarding data requirement 5.7, column B, it was noted that "(enough) data to calculate MRLs" are not necessary for performing a consumer risk assessment.
- The areas of concern, namely the fact that the risk assessment could not be performed due to missing data, and the variability of GAP, remain.

RMS is requested to append a 'list of uses supported by available data' instead of a 'list of intended uses' to the evaluation table.

PARATHION (continued)

6 Recommendations

Many data requirements are still open, many problems remain and several areas of concern were identified. COM will discuss bilaterally with the RMS how to proceed and will come quickly to a decision.

Annex 1: Revised evaluation table rev. 0-3 (including complete list of data requirements): parathion

Classification criteria for data requirements were discussed at the ECCO 100 meeting. The group agreed on having three criteria:

- Data requirements essential for unconditional Annex I inclusion;
- Data requirements to be dealt with at Member State level; and
- Data requirements fulfilled.

Annex 2: Complete list of end points: parathion

Annex 4: Suggested classification and labelling: parathion

WORKING DOCUMENT – DOES NOT NECESSARILY REPRESENT THE VIEWS OF THE COMMISSION SERVICES

1. Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

No	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
				Section 1 Data requirements: 13 Open points: 4
1.1	Physical and chemical properties: studies on B.2.1.1 to 2.1.10, 2.1.13, 2.1.21, 2.1.22, 2.1.23, 2.1.24, 2.1.25 are required (IIA 2.1 to 2.15). **A**	Spectra: Spectra are enclosed Oxidising Properties: Since the molecular structure does not contain reducing or oxidising moieties, we do not believe this study need to be conducted Remaining Requirements: We agree to conduct the studies. Reports to be available 9 months after the ECCO overview meeting.	UV spectrum: λ_{max} 275 nm. No peaks above 290 nm. Oxidising Properties : the statement can be considered acceptable.	Overview meeting (03. - 07.07.2000): See reporting table ECCO 89 (ii) for a comprehensive list of data required. Data essential for unconditional Annex I inclusion.
1.2	Statement on pH dependency and purity of the active substance in the study on solubility in water is required (IIA 2.6). **A**	We agree to conduct a study. Report to be available 9 months after the ECCO overview meeting.	Data will be submitted	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
1.3	Statement on pH dependency and the purity of the active substance in the study on partition coefficient is required (IIA 2.8). **A**	We agree to conduct a study. Report to be available 9 months after the ECCO overview meeting.	Data will be submitted	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
	Open point 1.1: rapporteur Member State (MS) to check data on hydrolysis rate on p. 16 (Vol. 1) and p. 21 (Vol. 3).		There is a discrepancy between the statements in Vol. 1 and Vol. 3. Parathion must be considered relatively stable in buffered aqueous solutions at 25°C.	Overview meeting (03. - 07.07.2000): Open point fulfilled.
	Open point 1.2: rapporteur MS to check data on direct phototransformation on p. 16 (Vol. 1) and p. 22 (Vol. 3).		There is a discrepancy between the statements in Vol. 1 and Vol. 3. Parathion must be considered moderately degradable by UV light.	Overview meeting (03. - 07.07.2000): Open point fulfilled.
1.4	Justification for the statement on flammability is required (IIA 2.11.1). A	We agree to conduct a study. Report to be available 9 months after the ECCO overview meeting.	Data will be submitted.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
1.5	Complete Annex III data package for one plant protection product is required (IIIA 2). A	We agree to update the Annex III dossier to a complete data package. This will be available 24 months after the ECCO overview meeting.	Data will be submitted.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
1.6	Details of uses and further information: more detailed information on section B.3.5 is required (IIIA 4). MS		No further information have been found.	Overview meeting (03. - 07.07.2000): See reporting table ECCO 89 (xv) for a comprehensive list of data required. Data essential for unconditional Annex I inclusion.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
	Open point 1.3: rapporteur MS to submit a list of uses supported by available data as soon as possible.		Data have been submitted. See list of end points updated in January 2000.	Overview meeting (03. - 07.07.2000): A list of "uses supported by available data" is required. Remaining open point.
1.7	Methods of analysis: further information on analytical methods including validation data relating to impurities in analysis of batches is required (IIA 4.1). **A**	We agree to submit adequate validation data. Data to be available 12 months after the ECCO overview meeting	Data will be submitted	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
1.8	New method of analysis for food and feed with independent laboratory validation is required (IIA 4.2.1). **A**	Plants: Adequate methods will be developed for residue studies to be conducted as a result of residue data gaps. Reports will be available 18 months after the ECCO overview meeting Animal Origin: Methodology was submitted on November 15, 1999 for milk, kidneys, liver and fat.	A methodology has been submitted on November 15, 1999 for milk and kidneys See endpoints updated May 2000 GLP : Yes The methodology includes validated methods for analysis of parathion, paraoxon and 4-acetamidoparaoxon in samples of animal origin. The methods show good recoveries and good reproducibility at the doses tested. The methods can be considered acceptable.	Overview meeting (03. - 07.07.2000): Residues have not been finally defined, therefore: Data essential for unconditional Annex I inclusion.
1.9	Address the applicability of a multi-residue method (IIA 4.2). **A**	We agree to develop a suitable method. Report to be available 18 months after the ECCO overview meeting.	Data will be submitted.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
1.10	New method of analysis for soil is required (IIA 4.2.2). A	We need to assess the comments from Germany, France and Greece before committing to develop a method.	Data will be submitted.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
1.11	New method with commonly available technique for drinking water and surface water is required (IIA 4.2.3). A	We agree to develop a method. Report to be available 18 months after the ECCO overview meeting.	Data will be submitted.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
	Message from ECCO 89 to ECCO 93: is the limit of determination for methods of analysis for air sufficiently low?			Message was discussed at ECCO 93 (see data requirement 4.8 and reporting table ECCO 93, xiii).
1.13	Propose new LOQ_{air} taking into consideration the new systemic AOEL (IIA 4.2.4). A	Cheminova A/S agrees to calculate a new LOQ_{air}. Suggested timeframe as in section 4.5.	-	Overview meeting (03. - 07.07.2000): This additional data requirement is the former data requirement 4.8, which was moved from section 4 to section 1. Data essential for unconditional Annex I inclusion.
1.12	New method for analysis of residues in wildlife and for use in support of diagnostic and therapeutic regimes is required (IIA 4.2.5). A	We agree to develop methods. Reports to be available 18 months after the ECCO overview meeting.	Data will be submitted.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
	Open point 1.4: rapporteur MS to amend list of end points: FAO specification, minimum purity, impurities, physical and chemical properties, list of uses supported by available data, methods of analysis and classification and labelling.		See endpoints updated May 2000.	Overview meeting (03. - 07.07.2000): Open point fulfilled.

2. Fate and Behaviour

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
				Section 2 Data requirements: 1 (6 removed) Open points: 0 (3 removed)
2.1	A full Annex II and Annex III data package for the fate and behaviour section is required.			Overview meeting (03. - 07.07.2000): This new data requirement was proposed at the meeting. The former data requirements 2.1 - 2.6 and the open points 2.1 - 2.3 were removed, because these points only reflected the missing data identified before the discussion on parathion at ECCO 91 was interrupted and finished (because of the extremely incomplete data package). Data essential for unconditional Annex I inclusion.
~~2.1~~	~~A new laboratory study on route of degradation in soil is required (IIA 7.1.1.1.1). A~~			
~~2.2~~	~~Data on degradation in soil under anaerobic conditions with regard to the intended uses in rice are required (IIA 7.1.1.2). A~~			
~~2.3~~	~~Regarding the formulation 3 laboratory studies concerning the rate of degradation in soil are required (IIA 7.1.1.2, IIIA 9.1.1). A~~			

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
~~2.4~~	~~Regarding the formulation 3 field studies concerning the rate of degradation in soil are required (IIA 7.1.1.2, IIIA 9.1.1) A~~			
	~~Open point 2.1: : rapporteur Member State to recalculate the PEC_{soil} values on the basis of the worst case of application.~~			
~~2.5~~	~~2 new water sediment studies are required (IIA 7.2.1). A~~			
	~~Open point 2.2: rapporteur Member State to recalculate the PEC_{sw} values on the basis of a 0.3 m depth water body.~~			
~~2.6~~	~~An Atkinson calculation concerning fate and behaviour in air is required (IIA 7.2.2, IIIA 9.3). A~~			
	~~Open point 2.3. rapporteur Member State to amend list of endpoints.~~			

3. Ecotoxicology

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
				Section 3 Data requirements: 13 Open points: 3
3.1	Information on acute toxicity of the active substance to mallard duck is required. (AII 8.1.1) A	A study on Bobwhite quail with a 500 g/L EC formulation is available. Information on the acute toxicity of parathion to birds is available in Hudson *et al.* (1984) which Cheminova will submit. In particular, the data presented in this reference indicates that the acute toxicity of parathion to the Mallard duck is similar to that for the Bobwhite quail. Cheminova considers that this provides information to meet this point.	RMS considers that the evaluation of these data could provide enough information on this point.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
	Open point 3.1: rapporteur MS to conduct risk assessment for birds and mammals for worst case conditions.	Cheminova agrees to conduct a comprehensive risk assessment for birds, incorporating a first-tier, worst-case risk assessment and then considering more realistic exposure and effects characterisation as appropriate, using the available data.	RMS will evaluate the risk assessment for worst case conditions (highest application rate, short grass) when provided by the notifier. So far the worst case exposure (short grass) has been considered and corresponding TERs have been included in the list of end points.	Overview meeting (03. - 07.07.2000): This open point was converted into new data requirements (see data requirements 3.12 and 3.13). Open point fulfilled.
3.12	Risk assessment for birds for worst case conditions is required. (AII 8.1)			Overview meeting (03. - 07.07.2000): This new data requirement was proposed at the meeting. Data essential for unconditional Annex I inclusion.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
3.13	Risk assessment for mammals for worst case conditions is required. (AIII 10.3)			Overview meeting (03. - 07.07.2000): This new data requirement was proposed at the meeting. Data essential for unconditional Annex I inclusion.
	Open point 3.2: rapporteur MS to check if monitoring studies on the effects on birds and mammals have been submitted.	Monitoring studies on the effects of parathion on birds and mammals have not been submitted.	No monitoring studies sofar submitted.	Overview meeting (03. - 07.07.2000): (see data requirement 3.2) Open point fulfilled.
3.2	Submit monitoring studies on effects on birds and mammals, if these studies have not yet been submitted to the rapporteur MS. (AII 8.1, AIII 10.3) A	Cheminova will conduct a literature search in order to identify any available avian/mammalian monitoring/incident data. The results of the literature search can be made available by **March 2001.** In addition, an assessment will be conducted to consider the relevance of this information to the proposed GAP for parathion in the EU.	Information from monitoring studies and assessment of their relevance will be evaluated when submitted.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
3.3	Depending on the final risk assessment on the available data, higher tier risk assessments for birds and mammals might be required. (AII 8.1, AIII 10.3) A	Cheminova accepts that it will probably be necessary to consider a higher tier risk assessment for birds and mammals. This will initially involve a stepwise risk assessment based on the currently available data (see open point 3.1) and on consultation with the rapporteur MS. Any additional requirements will depend on the outcome of this assessment.	RMS has recognized that, already from the preliminary assessment conducted, the need for a higher tier assessment arises: this assessment will be evaluated when provided by the notifier.	Overview meeting (03. - 07.07.2000): The meeting pointed out that it is very likely that higher tier risk assessment for birds and mammals will be required. Data essential for unconditional Annex I inclusion.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
3.4	Submit all available data on the toxicity of parathion to *Daphnia* sp. (AII 8.2.4) A	Cheminova agrees to conduct a literature search to identify any additional data on the toxicity of *Daphnia* spp. to parathion. As this data will be non-GLP, it will be assessed on the basis of its quality and consistency and incorporated into the risk assessment as appropriate. The results of the literature search can be made available by **March 2001.**	Data will be evaluated when submitted by the notifier and considered for the risk assessment if appropriate.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
	Open point 3.3: risk assessment for aquatic organisms to be recalculated as agreed on at the meeting.	Cheminova agrees that the aquatic risk assessment will be re-calculated according to current guidelines/recommendations i.e. using data for both the active ingredient and formulation together with the appropriate parameters. It will also consider appropriate refinements e.g. realistic exposure, mitigation measures, etc.	Risk assessment has been recalcuated as agreed on at the meeting (endpoints on active ingredients, correct PECs), see list of endpoints. However, it is still preliminary (no highest application rates). A completely readdressed assessment will be evaluated when provided by the notifier.	Overview meeting (03. - 07.07.2000): Remaining open point.
3.5	Address higher tier risk assessment for aquatic organisms. (AII 8.2 A	Cheminova agrees that the initial aquatic risk assessment is likely to identify a high risk to aquatic invertebrates. This will be addressed as part of a stepwise risk assessment based on current data (see open point 3.3) and on consultation with the rapporteur MS. Any additional requirements will depend on the outcome of this assessment.	The assessment will be evaluated when provided and in consultation with the notifier.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
3.6	Address higher tier risk assessment for bees. (AII 8.3.1) **A**	A higher tier risk assessment for bees will be addressed on the basis of the revised EPPO guidelines, the current GAP and in consultation with the rapporteur MS.	The assessment will be evaluated when provided and in consultation with the notifier.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
3.7	Address the risk to non-target arthropods: field tests are required. (AII 8.3.2, AIII 10.5.2) **A**	A risk assessment for non-target arthropods will be addressed taking into account the recommendations of the ESCORT 2 workshop and in consultation with the rapporteur MS.	The assessment will be evaluated when provided and in consultation with the notifier.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
3.8	Submit the available data on the reproductive toxicity to earthworms and information from field tests on earthworms. (AII 8.4.2, AIII 10.6.1.3) **A**	Cheminova will conduct a literature search on the effects of parathion on earthworms, including reproductive toxicity and field data. Any information found will be assessed on the basis of its quality and consistency. However, the risk assessment should initially be based on the currently available Tier 1 data, the proposed EU GAP and the known environmental profile for parathion before deciding on the need for higher tier data. The results of the literature search can be made available by **March 2001.**	RMS will evaluate the data when provided by the notifier.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
3.9	An activated sludge respiration inhibition test is required. (AIII 8.7) **MS**	An activated sludge respiration inhibition test will be conducted and reported by the end of 2001.	Data will be evaluated when provided.	Overview meeting (03. - 07.07.2000): Data to be dealt with at Member State level.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
3.10	Submit all available data on effects on non-target flora and fauna. (AII 8.6) MS	Cheminova believes that further data concerning the possible effects of parathion on non-target flora and fauna will not change the environmental risk assessment.	RMS considers the requirement needed in any case, according to the Directive.	Overview meeting (03. - 07.07.2000): Data to be dealt with at Member State level.
3.11	Consider if any data from the references given in the comment from the European Environmental Bureau can be used in the risk assessments. A	Cheminova will consider the data in the references given in the comment from the European Environmental Bureau.	The overall risk assessment will take into account the comments provided.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.

4. Mammalian toxicology

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
				Section 4 Data requirements: 7 (1 removed) Open points: 2
4.1	Developmental neurotoxicity study, including brain AChE inhibition, following peri-postnatal exposure to parathion is required (IIA 5.6.). A	In support of US registrations, a developmental neurotoxicity study is being conducted. Anticipated time schedule: Final protocol: July 1, 2000 In-life phase: Aug 30 - Dec 30, 2000 Final Report: June 1, 2001	A definitive conclusion should await the data from the planned study.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
4.2	No data on medical surveillance on manufacturing plant personnel are reported in the dossier. The lack of these data is not acceptable, since this product has been used for many years. A report on the results of medical surveillance of manufacturing workers is required, including results of biological monitoring (IIA 5.9). A	Reports addressing this data requirement were included in "Addendum to Dossier to Include New Studies" submitted on January 17, 2000 to the ECCO -TEAM and the RMS.	The applicant has provided the information required.	Overview meeting (03. - 07.07.2000): Data requirement fulfilled.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
4.3	Comprehensive information is missing concerning accidental or occupational cases of acute poisoning, and epidemiological results on the occupational or general population. The lack of these data is not acceptable for a product which has been used for many years. Further information on these issues is required (IIA 5.9). **A**	Reports addressing this data requirement were included in "Addendum to Dossier to Include New Studies" submitted on January 17, 2000 to the ECCO -TEAM and the RMS	The applicant has provided the information required.	Overview meeting (03. - 07.07.2000): Data requirement fulfilled.
4.4	Provide NOAEL for hippocampal AChE inhibition in female rats following subchronic administration (IIA 5.10). **A**	An explanation of female hippocampal AChE inhibition is given in Appendix A. The methyl parathion study referenced in Appendix A can be submitted on short notice if study will be needed for evaluation.	The explanation provided by the applicant is deemed satisfactory. The observed reduction of hippocampal AchE is a chance finding, not treatment-related. There is no need, in the opinion of the Rapporteur, to submit the methyl parathion study.	Overview meeting (03. - 07.07.2000): Data requirement fulfilled.

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No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
4.5	New operator exposure estimations, taking into consideration the new AOEL and appropriate dermal absorption rate is required (IIIA 7.2.1). A	Cheminova A/S agrees to calculate new operator exposure estimates. Suggested timeframe: Two to three months after intended uses has been defined (ECCO overview meeting). However, we would like to comment briefly on the rejection of the human volunteer data for setting of the AOEL. We believe it is justifiable to consider the human data for the following reasons: 1) The human volunteer studies evaluated in the monograph results in very similar no effect levels for cholinesterase inhibition and the dosing regimes were appropriate for AOEL setting. 2) Other authorities and institutions have utilised the human data for risk assessment. Further information is provided in Appendix B.	Any conclusion should await the results of the new operator exposure estimates. Due to the significant neurotoxicity of Parathion, the Rapporteur supports a conservative approach using comprehensive animal studies to define the ADI and AOEL. Thus, the applicant does not support the utilisation of limited human data for setting the AOEL.	Overview meeting (03. - 07.07.2000): "Uses supported by available data" to be stated by main data submitter. Safe uses to be identified. Data essential for unconditional Annex I inclusion.
4.6	Worker exposure estimations are required, taking into consideration the new AOEL and appropriate dermal absorption rate (IIIA 7.2.3). A	Cheminova A/S agrees to calculate new worker exposure estimates. Suggested timeframe as in section 4.5.	Any conclusion should await the results of the new worker exposure estimates.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
4.7	Bystander exposure estimations are required (IIIA 7.2.2). A	Cheminova A/S agrees to calculate bystander exposure estimates. Suggested timeframe as in section 4.5.	Any conclusion should await the results of the new bystander exposure estimates.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
4.8	~~Propose new LOQ_{air} taking into consideration the new systemic AOEL (IIA 4.2.4). A~~	~~Cheminova A/S agrees to calculate a new LOQ_{air}. Suggested timeframe as in section 4.5.~~	-	Overview meeting (03. - 07.07.2000): This data requirement was moved to section 1 (see data requirement 1.13).
	Open point 4.1: rapporteur Member State (MS) to a draft new text proposal for chapter 2.7.2 on residues relevant for worker safety when the result of data requirement 4.6 is available.	-	-	Overview meeting (03. - 07.07.2000): Remaining open point.
	Open point 4.2: rapporteur MS to amend list of end points.	-	-	Overview meeting (03. - 07.07.2000): A revised list of end points will be submitted for the Full Report. Open point fulfilled.

5. Residues

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
				Section 5 Data requirements: 7 Open points: 2
5.1	A plant residue definition for monitoring and for risk assessment is required. IIA 6.1 and 6.7, IIIA 8.1 and 8.6 A	The plant metabolism studies carried out on three different crop groups indicate that there are no significant metabolites. However, paraoxon is known to be acutely toxic. For this reason, parathion and paraoxon should be regarded as the residues of concern.	The statement cannot be accepted because the metabolism studies were not conducted on crops considered for supported uses. No other studies have been submitted.	Overview meeting (03. - 07.07.2000): RMS to evaluate new metabolism studies. Data essential for unconditional Annex I inclusion.
5.2	An animal residue definition for monitoring and for risk assessment is required. IIA 6.2 and 6.7, IIIA 8.1 and 8.6 A	Metabolism and distribution studies in cows, goats and pigs have shown that parathion is extensively metabolised. In ruminants, the end product is p-nitro-phenol. In view of the formation of paraoxon as an acutely toxic metabolite, the animal residue definition should be regarded as parathion and paraoxon.	Available studies were not consideres acceptable at the ECCO 97 Meeting. No other studies have been submitted.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
5.3	Studies on the stability of residues are required. IIA 6 and 8 MS	Cheminova will carry out storage stability studies relevant to the proposed GAP, the results of which will be available 3 years after the ECCO overview meeting.	Studies will be submitted.	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
5.4	Data on residues in livestock feeding studies are required. IIA, 6.4, IIIA 8.3 **MS** The requirement 5.4 depends on the evaluation of the available studies on metabolism in livestock.	Residues in tissues and milk from livestock metabolism studies were low, so a livestock feeding study was not conducted. However, Cheminova are willing to conduct a livestock feeding study if this is considered necessary.	See point 5.2	Overview meeting (03. - 07.07.2000): Data essential for unconditional Annex I inclusion.
5.5	Explanation and clarification on the wide range of GAP`s is needed. IIA, 6.3, IIIA 8.2. A	Cheminova have now drastically reduced the number of crops in the GAP and the Monograph has been revised based on the new GAP. In addition, a further revised GAP was sent to the Rapporteur on 03 May 2000. This is attached as Appendix 1. If further clarification is required, Cheminova are prepared to discuss this with the Rapporteur.	Gap's have been updated. See updated endpoints.	Overview meeting (03. - 07.07.2000): Data requirement fulfilled.
5.6	Sufficient residue trials covering GAP are required taking into account results from metabolism studies in plants. IIA 6.3, IIIA 8.2 **MS**	Cheminova acknowledges the residue trial requirements stated in the Monograph and will carry out the trials specified. The results will be available by July 2002.	Studies will be submitted.	Overview meeting (03. - 07.07.2000): Data to be dealt with at Member State level.
5.7	Consumers risk assessment is required. IIA 6.9, IIIA 8.8	At present there is insufficient data to calculate MRLs. Once the residues data have been generated, the consumer risk assessment will be carried out.	Acceptable. ***RMS, please amend the ADI in section 5 of the list of end points according to the value given in section 4.***	Overview meeting (03. - 07.07.2000): A consumer risk assessment can be performed even if there are not enough data to set MRL's. Data essential for unconditional Annex I inclusion.

No.	Column A Conclusions of the ECCO-Peer Review Meeting	Column B Comments from the main data submitter / applicant on the ECCO-Review conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group
	Open point 5.1: RMS to reassess data on processing factors.		Data on processing factors will be reassessed after the residue definition.	Overview meeting (03. - 07.07.2000): Remaining open point.
	Open point 5.2: RMS to amend the list of end points.		List of endpoints has been amended.	Overview meeting (03. - 07.07.2000): Open point fulfilled.

Areas of concern

Section 1: very incomplete data set for Annex II and III.

Section 2: not discussed.

Section 3: risk to birds, aquatic organisms, bees and non-target arthropods;
lack of information on the metabolites;
incomplete risk assessments because of missing data on exposure.

Section 4: AOEL is exceeded for operators;
high risk of acute poisoning by all routes of exposure.

Section 5: the risk assessment could not be performed due to the missing data;
variability of GAP.

Summary of intended uses (active substance)

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
apple	France		F	biting and suckling insects	EC	93	spraying		1-2		0.0186		0.186	15	
	Portugal		F	biting and suckling insects	EC	500	spraying		1-3		0.02-0.03		0.2-0.3	21	
	Portugal		F	biting and suckling insects	WP	200	spraying		1-3		0.02		0.2	21	
Cereals	Northern Europe		F	Tipula	EC	500	Foliar spray	Autumn Spring	1 1			400 - 600	0.15 - 0.225	NA	PHI covered by vegetation period. Maximum two application s per season.
citrus fruit	Italy		F	biting and suckling insects	EC	200	spraying		1		0.016-0.025		0.24-0.375	20	
grape	France		F	biting and suckling insects	EC	93	spraying		1		0.0465		0.465	15	insects pass the winter

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
	Germany		F	biting and suckling insects	EC	100	spraying		1		0.05		0.3	-	water rate depending on experiences of region; apply from growth - stage 0.1-0.5
	Germany		F	biting and suckling insects	EC	500	spraying		1		0.0175		0.14	28	water rate depending on experiences of region
	Italy		F	biting and suckling insects	EC	200	spraying		1-2		0.016-0.025		0.16-0.25	20	
	Portugal		F	biting and suckling insects	EC	500	spraying		1-2		0.02-0.03		0.2-0.3	21	
	Portugal		F	biting and suckling insects	WP	200	spraying		1-2		0.02-0.04		0.2-0.4	21	
	Spain		F	biting and suckling insects	EC	30	spraying		1		0.0225-0.06		-	NA	Insect pass the winter, no practical use
	Spain		F	biting and suckling insects	EC	50	spraying		1		0.05		0.75	-	no practical use

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
peach	Belgium		F	biting and suckling insects	EC	250	spraying		1		0.175		0.0525	21	
	Belgium		F	biting and suckling insects	EC	250	spraying		1		0.175		0.2625	21	
	France		F	biting and suckling insects	EC	93	spraying		1-2		0.0186		0.186	-	
	Portugal		F	biting and suckling insects	EC	500	spraying		1-2		0.02-0.03		0.2-0.3	21	
	Portugal		F	biting and suckling insects	WP	200	spraying		1-2		0.02		0.2	21	
pear	Portugal		F	biting and suckling insects	EC	500	spraying		1-2		0.02-0.03		0.2-0.3	21	
	Portugal		F	biting and suckling insects	WP	200	spraying		1-2		0.02		0.2	21	
pomefruit	Germany		F	biting and suckling insects	EC	100	spraying		1		0.05		0.75	NA	do not apply below +5°C
	Italy		F	biting and suckling insects	EC	200	spraying		1		0.016-0.025		0.24-0.375	20	

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
	Spain		F	biting and suckling insects	EC	30	spraying		1		0.0225-0.06		0.3375-0.9	21	insects pass the winter
	Spain		F	biting and suckling insects	EC	50	spraying		1		0.05		0.75	21	
	Spain		F	biting and suckling insects	EC	200	spraying		2-3		0.03-0.04		0.45-0.6	21	
stone fruit	Germany		F	biting and suckling insects	EC	500	spraying		1		0.05		0.75	NA	do not apply below +5 °C
	Italy		F	biting and suckling insects	EC	200	spraying		1		0.016-0.025		0.24-0.375	20	
	Spain		F	biting and suckling insects	EC	30	spraying		1		0.0225-0.06		0.3375-0.9	21	insects pass the winter
	Spain		F	biting and suckling insects	EC	50	spraying		1		0.05		0.75	21	
	Spain		F	biting and suckling insects	EC	200	spraying		2-3		0.03-0.04		0.45-0.60	21	

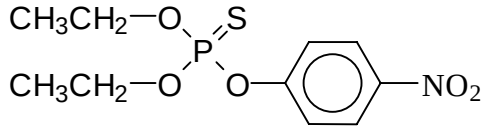
Annex 2

COMPLETE LIST OF END POINTS: **PARATHION**

1 Physical chemical properties section

Active substance (ISO Common Name)	Parathion
Function (*e.g*. fungicide)	Insecticide
Rapporteur Member State	Italy

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	O,O-diethyl O-4-nitrophenyl phosphorothioate
Chemical name (CA)	O,O-=diethyl O-(4-nitrophenyl) phosphorothioate
CIPAC No	0010
CAS No	56-38-2
EEC No (EINECS or ELINCS)	015-034-00-1 (200-271-7)
FAO Specification (including year of publication)	Min 950 g/kg ± 20 g (10.b/TC/S 1989)
Minimum purity of the active substance as manufactured (g/kg)	960
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	Ethylparaoxon 1.331 g/kg
Molecular formula	$C_{10}H_{14}NO_5PS$
Molecular mass	291.3 g/mol
Structural formula	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity)	Data required
Boiling point (state purity)	Data required
Temperature of decomposition	Data required
Appearance (state purity)	Data required
Relative density (state purity)	Data required
Surface tension	64.9 mN/m (20 ppm at 21°C) (Purity not stated)
Vapour pressure (in Pa, state temperature)	Data required
Henry's law constant (Pa m^3 mol^{-1})	0.0302 Pa.m^3/mol (Purity not stated)
Solubility in water (g/l or mg/l state temperature)	GLP: Yes 12.4 ± 0.7 mg/l at 25 ± 1°C (Purity: data required) (pH dependency: data required)
Solubility in organic solvents (in g/l or mg/l state temperature)	Data required
Partition co-efficient (log P_{ow}) (state pH and temperature)	GLP: Yes 1598 (log K_{ow} = 3.15 ± 0.27) (Purity not stated)

Hydrolytic stability (DT_{50}) (state pH and temperature)	GLP: Yes
	pH 5, 0.2 M acetic acid and 0.2 M sodium acetate (acetate buffer);
	pH 7 (t), 0.2 M tris(hydroxymethyl)aminomethane and 0.2 M HCl (tris buffer);
	pH 7(H), 0.01 M N-2-hydroxyethylpiperazine-N'-2-ethanesulphonic acid and 0.2 M KOH;
	pH 9, 0.2 M boric acid and 0.2 M sodium borate (borate buffer).
	
	Hydrolysis of ^{14}C-Parathion at 25°C
	
	pH — Rate Constant ($days^{-1}$) — Half-life (days)
	5 — -0.00520 — 133
	7H — -0.00280 — 247
	7t — -0.00194 — 356
	9 — -0.00678 — 102
	
	One degradation product appeared in all buffer systems but accounted for <2% of activity at pH 5 or 7 and 9% at pH 9.
	(Purity not stated)

Dissociation constant	No dissociation in water
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	275 nm (Purity not stated) (ε not submitted)

Photostability (DT_{50}) (aqueous, sunlight, state pH)	GLP: Yes The calculated rate constant and half-life for the non-sensitised exposed system were -0.0230 $days^{-1}$ and 30 days, respectively, and -0.00341 $days^{-1}$ and 203 days, respectively, for the non-sensitised dark samples. The rate constant for the sensitised exposed system was determined to be -156 $days^{-1}$ giving a half-life of 44 days. For the sensitised dark system, a rate constant of -0.00085 $days^{-1}$ was calculated, giving a half-life of 811 days. Aqueous photochemical degradation products identified were paraoxon, 4-nitrophenol, S-ethyl or S-phenyl parathion, hydroquinone and 4-nitrosophenol.
Quantum yield of direct phototransformation in water at $\sum$ > 290 nm	GLP: Yes 3.0×10^{-5}
Flammability	Not classified as a flammable liquid. Auto-ignition temperature: 340°C (Purity not stated)
Explosive properties	Parathion is not explosive.

Methods of Analysis

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

Technical as (principle of method)	Method: Analytical Method VAM 003-01 and validation VAMR 003-01. GLP: Yes GC-TCD Linearity: correlation coefficient = 0.99997. Limit of determination: Not stated. Specificity: specific when chromatographed: methyl parathion, alkylisoparathion. Interferences: not stated. Inter-lab accuracy: not stated Repeatability: Precision expressed as Coefficient of variation (n = 25) was 0.5%.
Impurities in technical as (principle of method)	
Plant protection product (principle of method)	See **Technical as**

Analytical methods for residues (Annex IIA. point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Data required
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Indipendent Laboratory Validation of Methodology for the analysis of Ethyl Parathion, Ethyl Paraoxon, and 4-acetamidoparaoxon (4-AA) in kidney and Milk. According to PR notice 96-1 and OPPTS 860.1340 Guidelines. B.B Williams, 1998 GLP: YES Milk: samples added with acetone/dichloromethane were portioned against water. Organic phases were purified by Chem Elut column. Kidney: samples added with acetone/water/ dichloromethane were filtered and the extracts were portioned against water. Organic phases were cleaned-up on C18 SPE column. Determination: GC/FPD Linearity: not reported Precision: not determined Accuracy: - Milk mean recoveries (samples fortified at 1-2 µg/kg): parathion (93% ± 4), ethyl paraoxon (87% ± 5), 4-AA (94% ± 5) - Kidney mean recoveries (samples fortified at 10 – 20 µg/kg): parathion (103% ± 13), ethyl paraoxon (87% ± 11), 4-AA (82% ± 9) Specificity: no interferences with co-extractables. LOQ: Milk, 1µg/kg; Kidney, 10 µg/kg
Soil (principle of method and LOQ)	Data required

Water (principle of method and LOQ)	Data required
Air (principle of method and LOQ)	GLP: Yes Adsorption tube: two adsorption layers (Tenax and XAD-2). Extraction: ultrasonication with n-butylacetate GC – NPD detector Linearity: 0.069 – 0.550 mg/l (0.0046 – 0.229 mg a.i./m^3) C.V. = 0.998. Limit of determination: 0.0046 mg a.i. /m^3. Specificity: not stated. Interferences: none stated. Inter-lab accuracy: not stated. Repeatability: recoveries were in the range 80.8 – 101%.
Body fluids and tissues (principle of method and LOQ)	Data required

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	

Annex 2

COMPLETE LIST OF END POINTS: **PARATHION**

2 Fate and behaviour section

No data submitted.

Annex 2

COMPLETE LIST OF END POINTS: **PARATHION**

3 Ecotoxicology section

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

Acute toxicity to mammals	LD50 2.4 mg/kg bw rat oral
Acute toxicity to birds	LD50 2.7 mg/kg bw bobwhite quail
Dietary toxicity to birds	LC50 76 ppm mallard duck
Reproductive toxicity to birds	NOEC 2.85 ppm mallard duck
Long term toxicity to mammals	NOEL 0.25 mg/kg bw rat developmental toxicity

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
0.3-0.2	orchard, vines/arable	small bird	acute	1.8-2.7	10
0.3-0.2	orchard, vines/arable	small herbivorous bird	acute	0.27-0.4	10
0.3-0.2	orchard, vines/arable	large bird	acute	5-7.7	10
0.3-0.2	orchard, vines/arable	small bird	short term	16-24	10
0.3-0.2	orchard, vines/arable	small herbivorous birds	short term	2.3-3.4	10
0.3-0.2	orchard, vines/arable	large bird	short term	14-22	10
0.3-0.2	orchard, vines/arable	small bird	long term	0.6-0.9 (0.7-1.1°°)	5
0.3-0.2	orchard, vines/arable	small herbivorous birds	long term	0.08-0.13	5
0.3-0.2	orchard, vines/arable	large bird	long term	0.53-0.81 (0.67-1°°)	5
0.3-0.2	orchard, vines/arable	small mammal	acute	1.6-2.4	10
0.3-0.2	orchard, vines/arable	small herbivorous mammal	acute	0.28-0.43	10
0.3-0.2	orchard, vines/arable	large mammal	acute	4.5-6.8	10
0.3-0.2	orchard, vines/arable	small mammal	long term	1.45-2.2	5
0.3-0.2	orchard, vines/arable	small herbivorous mammal	long term	0.03-0.04	5
0.3-0.2	orchard, vines/arable	large mammal	long term	4.1-6.1	5

Assumptions for the diet:
small birds and small mammals: equal quantities of small insects and large insects (calculated ETE of 3.2-4.8 ppm)
large birds and large mammals: 10% leaves+45% small insects+45%large insects (calculated ETE of 3.5-5.3 ppm)

herbivorous birds and mammals: 100% short grass

°°TERs which take into account the degradation of residues assumed (79% of initial after 5 days)

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				
Golden orfe	a s	96 hours	LC_{50} NOEC	0.58 mg a.i./l <0.2 mg a.i./l
Rainbow trout	formulation (102 g/l EC)	96 hours	LC_{50} NOEC	1.02 mg a.i./l <0.6 mg a.i./l
Daphnia magna	a s	48 hours	EC_{50} NOEC	2.5 µg a.i./l <1.0 µg a.i./l
Daphnia magna	formulation (76.4% EC)	48 hours	EC_{50} NOEC	2.4 µg a.i./l 1.1 µg a.i./l
Scenedesmus subspicatus	a s	96 hours	48h EC_{50} NOEC	0.5 mg a.i./l 0.1 mg a.i./l
Scenedesmus subspicatus	formulation (47.4% EC)	96 hours	E_bC_{50} NOEC	0.47 mg a.i./l 0.3 mg a.i./l
Sheepshead minnow	a s	28 days	NOEC	0.72 µg a.i./l
Daphnia magna	a s	21 days	NOEC	0.56 µg a.i./l
Daphnia magna	formulation (47.4% EC)	21 days	NOEC	0.01 µg a.i./l
Daphnia magna	formulation (99 g/l EC)	21 days	NOEC	0.19 µg a.i./l
Microcosm or mesocosm tests: not performed				

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
0.2	Arable crops	Rainbow trout	96 h	5	1450	100
0.3	Vines	Rainbow trout	96 h	15	725	100
0.3	Orchards	Rainbow trout	96 h	15	232	100
0.2	Arable crops	*Daphnia magna*	48 h	5	6.3	100
0.3	Vines	*Daphnia magna*	48 h	15	3.1	100
0.3	Orchards	*Daphnia magna*	48 h	15	1	100
0.2	Arable crops	*Scenedesmus subspicatus*	96 h	5	1250	10
0.3	Vines	*Scenedesmus subspicatus*	96 h	15	625	10
0.3	Orchards	*Scenedesmus subspicatus*	96 h	15	200	10
0.2	Arable crops	Sheepshead minnow	21 d	5	1.8	10
0.3	Vines	Sheepshead minnow	21 d	15	0.9	10
0.3	Orchards	Sheepshead minnow	21 d	15	0.3	10
0.2	Arable crops	*Daphnia magna*	21 d	5	1.4	10
0.3	Vines	*Daphnia magna*	21 d	15	0.7	10
0.3	Orchards	*Daphnia magna*	21 d	15	0.2	10

TERs calculation has been based on the end points obtained with the active substance and the initial PECs (30 cm depth) of 0.4, 0.8, 2.5 µg/l for arable crops, vines and orchards.

Bioconcentration

Bioconcentration factor (BCF)	430
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50}) (CT_{90})	CT_{50} 1-3 days
Level of residues (%) in organisms after the 14 day depuration phase	1%

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

Acute oral toxicity	24 h LD50 0.1 g a.i./bee 24 h LD50 0.197 g form (500 g/L EC)/bee
Acute contact toxicity	24 h LD50 0.066 g a.i./bee 24 h LD50 0.131 g form (500 g/L EC)/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				
0.3	Orchards, vines	Oral	3000	50
0.3	Orchards, vines	Contact	4545	50

Field or semi-field tests
Not performed

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests						
Not available						

Field or semi-field tests
Not performed

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

Acute toxicity	14-day LC50 65 mg a.i./kg, NOEC 32 mg a.i./kg 14-day LC50 ≥ 105 mg a.i./kg, NOEC 1 mg a.i./kg (99 g/l EC) 14-day LC50 253 mg a.i./kg, NOEC 15.2 mg a. i./kg (47.4% EC)
Reproductive toxicity	not performed

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

Application rate (kg as/ha)	Crop	Time-scale	TER*	Annex VI Trigger
0.2	arable crops	14 d	≥404	10
0.2	arable crops	14 d	250	10
0.3	orchards, vines	14 d	≥262	10
0.3	orchards, vines	14 d	162	10

TERs have been calculated dividing the two LC50 of 65 and ≥105 mg a.i./kg by the initial PECs in soil of 0.13 and 0.2 mg a.i./kg; they have also been further divided by a factor of 2 to take into account the difference in organic matter content between artificial test soils and agricultural soils (being the logP >2).

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

Nitrogen mineralization	no significant effect up to 20 kg a.i./ha in silty sand and loamy silt soil, up to 2.5 kg a.i./ha in loamy sand and sandy silt soil
Carbon mineralization	no significant effect up to 20 kg a.i./ha in silty sand and loamy silt soil, up to 2.5 kg a.i./ha in loamy sand and sandy silt soil

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N, R 50/53

Annex 2

COMPLETE LIST OF END POINTS: **PARATHION**

4 Mammalian toxicology section

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

Rate and extent of absorption:	Rapid (>90%, based on urinary excretion)
Distribution:	Widely distributed.
Potential for accumulation:	No potential of accumulation.
Rate and exent of excretion:	Rapid, >99% within 48 hours, mainly via urine (86-94%)
Metabolism in animals	Extensively metabolised: desulfurization, dealkylation, conjugation, oxidation.
Toxicologically significant compounds (animals, plants and environment)	Parent compound and Paraoxon-ethyl.

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral	2-22 mg/kg/ bw (T+ R28)
Rat LD_{50} dermal	71-100 mg/kg bw (T R24)
Rat LC_{50} inhalation	0.03mg/l air (nose only) (T+ R26)
Skin irritation	Not irritant
Eye irritation	Not irritant
Skin sensitization (test method used and result)	Not sensitiser (M & K)

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect	Nervous system, inhibition of acetylcholinesterase activity
Lowest relevant oral NOAEL / NOEL	0.4 mg/kg bw (Dog 1 year) (NOAEL, according to JMPR criteria)
Lowest relevant dermal NOAEL / NOEL	0.1 mg/kg bw (Rabbit, 21-day)
Lowest relevant inhalation NOAEL/NOEL	0.00025 mg/l air (Rat, 21-day, nose only)

Genotoxicity (Annex IIA, point 5.4)	Weight of the evidence indicates no genotoxic potential.

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

Target/critical effect	Nervous system (inhibition of acetylcholinesterase activity); eye (retinal atrophy).

Lowest relevant NOAEL/NOEL	0.4 mg/kg bw (2 year rat)
Carcinogenicity	No carcinogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect	Reduced pup survival and body weight at parental toxic doses
Lowest relevant reproductive NOAEL/NOEL	1 mg/kg bw (rat, 2-generation)
Developmental target / critical effect	Reduced pup survival and body weight at parental toxic doses
Lowest relevant developmental NOAEL/NOEL	Overall NOAEL 0.25 mg/kg bw (rat)

Neurotoxicity/Delayed neurotoxicity (Annex IIA, point 5.7)

…… ……..	No evidence of delayed neurotoxicity in hens. Acute neurotoxicity (rat) NOAEL 0.5 mg/kg bw in females (< 2.5 mg/kg bw in males) based on functional operational battery (FOB). 13 week neurotoxicity NOAEL 0.06 mg/kg bw in males; 0.08 mg/kg bw in females, based on FOB and inhibition of brain acetylcholinesterase (R48). No data on developmental neurotoxicity; data required.

Other toxicological studies (Annex IIA, point 5.8)

…… ……..	Major metabolite (Paraoxon) is rapidly formed in animals and it is responsible for toxicity of Parathion. 28-day human oral NOEL 0.06 mg/kg bw (based on inhibition of erythrocyte cholinesterase)

Medical data (Annex IIA, point 5.9)

Inhibition of cholinesterase activity ollowing occupational and accidental exposures

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI	0.0006 mg/kg bw/day	13 week-neurotoxicity, rat	100
AOEL	0.0006 mg/kg	13 week-neurotoxicity,	100

	bw/day	rat	
Drinking water limit	Not considered by ECCO		
ArfD (Acute Reference Dose)	0.005 mg/kg bw	Acute Neurotoxicity, rat	100

Dermal absorption (Annex IIIA, point 7.3)

…… ……	9.7% for non occluded skin (human in vivo, 24 hours response).

Acceptable exposure scenarios (including method of calculation)

Operator	Not acceptable for proposed uses (German model, PPE)
Workers	No data. Information required
Bystanders	No data. Information required

Classification and proposed labelling (Annex IIA, point 5.9)

T+, R24, R26, R28, R48

Ministero della Sanità

Piazzale Marconi, 25

00144 Rome

Italy

Parathion

Volume 1

Report and Proposed Decision

CONTENTS

LEVEL 1

Parathion

Statement of subject matter and purpose for which the monograph was prepared

1.1 Purpose of the monograph (Document A)

Council Directive 91/414/EEC established a review programme for all active substances on the community market by 25 July 1993. This monograph on the review of parathion has been prepared for submission to the Standing Committee on Plant Health to enable a decision to be made on the listing of parathion on Annex 1 of the Directive 91/414/EEC.

1.2 Identity of the active substance (Annex II A 1)

1.2.1 Name and address of applicant(s) for inclusion of the active substance in Annex I (Annex II A1.1)

1.2.2 ISO common name and synonyms (Annex II A 1.3)

ISO: Parathion
Synonym: Ethyl parathion

1.2.3 Chemical name (Annex II A 1.4)

IUPAC: O,O-Diethyl O-(4-nitrophenyl) phosphorothioate

CA: Phosphorothioic acid, O,O-diethyl O-(4-nitrophenyl) ester

1.2.4 Manufacturer's development code number (Annex II A l.5)

EP-3 and E605

1.2.5 CAS, ECC and CIPAC numbers (Annex II A 1.6)

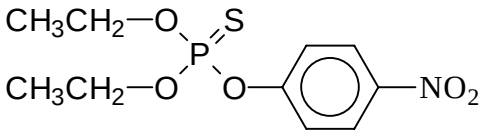
CAS number: 56-38-2
EEC number: 015-034-00-1

EINECS number: 200-271-7
CIPAC number: 0010

1.2.6 Molecular formula, molecular mass and structural formula (Annex II A 1.7)

Molecular formula: $C_{10}H_{14}NO_5PS$

Structural formula:



Molecular mass: 291.3 g/mol

1.2.7 Manufacturer of the active substance (Annex II A 1.2)

1.2.8 Method or methods of manufacture (Annex II A 1.8)

Confidential information, see Annex C

1.2.9 Specification of the purity of the active substance (Annex II A 1.9)

Characteristics	Typical g/kg	Upper Limit g/kg	Lower Limit g/kg	Analytical method
Parathion	≥ 960	1001	974	AM 52.1

1.2.10 Identity of inactive isomers, impurities and additives (Annex II A 1.10)

Confidential information, see Annex C

1.2.11 Analytical profile of batches (Annex II A 1.11)

Confidential information, see Annex C

1.3 Identity of the plant protection product Ethyl parathion EC formulations(Annex II A 3.1; Annex III A 1)

1.3.1 Current, former and proposed trade names and development code numbers (Annex III A 1.3)

Trade name: Ethyl parathion 100 EC; Ethyl parathion 500 EC

1.3.2 Manufacturer or manufacturers of the plant protection product (Annex III A 1.2)

Ethyl parathion 100 EC

Ethyl parathion 500 EC

1.3.3 Type of the preparation and code (Annex III A l.5)

Physical state: Emulsifiable concentrate (EC)

1.3.4 Function (Annex III A 1.6)

Insecticide.

1.3.5 Composition of the preparation (Annex III A 1.4)

Confidential information, see Annex C

1.4 Uses of the plant protection product Ethyl parathion

1.4.1 Fields of use (Annex II A 3.3; Annex III A 3.1)

Agriculture, horticulture, forestry, viticulture.

1.4.2 Effects on harmful organisms (Annex II A 3.2; Annex III A 3.2)

Almost all insect pests with sucking or biting mouth parts are controlled by parathion acting as a contact, stomach and inhalation poison.

Parathion is an organophosphorus insecticide with acaricidal and ovicidal effect. The mode of action of OP pesticides, whereby transmission of nerve impulses is blocked at the nerve synapses, is well documented (A.T. Eldefrawi, (1985), 'Acetylcholinesterases' in: Comprehensive insect physiology biochemistry and pharmacology, Vol. 12, Insect control, G.A. Kerkut, L.I. Gilbert (eds.), Pergamon Press pp 115 - 129). In brief, nerve impulses are transmitted to the next fibre (or to a muscle) by acetylcholine being released from the transmitting nerve, which stimulates the receiving nerve (muscle). The acetylcholine is then immediately catabolised by the enzyme acetylcholinesterase. The OP insecticides bind to acetylcholinesterase so that acetylcholine cannot be catabolised. Consequently control via the nervous system is blocked by nerves being permanently stimulated.

1.4.3 Summary of intended uses (Annex II A 3.4; Annex III A 3.3 to 3.7, 3.9)

Table 1.4.3-1 Harmful organisms controlled by Ethyl parathion EC formulations

Crop	Disease or pest controlled	Country
Agriculture - field crops		See Table 1.4.3-2
Horticulture - field crops	Biting insects	
Horticulture protected crops	Biting insects	
Horticulture - hops		
Horticulture - top fruit	Biting pests	

Viticulture	*Clysia ambiguella*	

Table 1.4.3-2 Summary of intended/approved uses of Ethyl parathion EC formulations

Crop/pest controlled	**Country**	**Maximum rate per application (kg a.i./ha)**	**Maximum rate per season (kg a.i./ha)**	**Maximum number of applications per season**	**Pre-harvest interval in days**	**Spray interval in days**
Biting insects	Belgium	0.525	1.05	2	21 or 28	*
Biting pests	France	0.465	0.465	2	15	*
Clysia	Germany	0.75	0.75	1	NA	*
ambiguella	Greece	0.5	0.9	3	14	*
	Italy	1.05	1.05	1	20	*
	Netherlands	0.244	0.366	2	20 - 28	*
	Portugal	0.4	0.9	3	21	*
	Spain	0.9	1.8	3	21	*

* spray interval is dependant on level of infestation

1.4.4 Information on authorisations in EU Member States (Annex III A 12.1)

Table 1.4.4-1 Authorisations and Registrations in the EU - Ethyl Parathion EC formulations

Country	Type of authorisation	Crops/uses	Authorisation details
Belgium	commercial	sugar beet beets linseed fruit leeks ornamental plants ornamental shrubs peaches rape vegetables	E 605 250 g/l EC Reg No: 4139
France	commercial	apple beets grapes ornamental plants peaches pummelo rape	Oleo-Bladen 93 g/l EC Reg No: 5400261
Germany	commercial	alfalfa barley climbing bean field bean kidney bean fodder beet sugar beet beets red cabbage white cabbage savoy cabbage cauliflower clover cucumber	E 605 forte 500 g/l EC Reg No: 21437

		grapes grassland kale kohlrabi leeks lettuce lupin oats ornamental plant ornamental shrub field pea potato rape rye spinach strawberry tomato turnip wheat	
		barley beech berries Douglas fir grapes ornamental shrub pome fruit spruce stone fruit strawberries	Folidol OEL 100 g/l EC Reg No: 21433
Germany	commercial	barley kidney bean fodder beet sugar beet Brussels sprouts red cabbage white cabbage savoy cabbage cauliflower kohlrabi lettuce	Ecombi 375 g/l EC Reg No: 21409

		oats garden peas potato rye spinach wheat	
Greece	commercial	grapes pome fruit stone fruit vegetables	Folidol E 605 200 g/l EC Reg No: 1001
		grapes pome fruit	Folidol OEL 100 g/l EC Reg No: 1248
Italy	commercial	artichoke asparagus aubergine barley bean broad bean beets cabbage carrots citrus fruit cotton cucumber garlic gourd grapes lettuce maize/corn melon water melon mixed forest olive onion ornamental plant garden pea pepper pome fruit	E 605 FT 20 200 g/l EC Reg No: 2411

		poplar potato rice spinach stone fruit strawberry tobacco tomato turnip wheat courgette	
Netherlands	commercial	alfalfa apple broad bean tick bean sugar beet beetroot blackberry cabbage cereals sour cherry clover blackcurrant redcurrant endive linseed fruit grapes grassland leeks lettuce maize/corn nuts onion ornamental plants field peas peaches pears plums potato	Folidol E0605 Geconc 250 g/l EC Reg No: 5492 N

		rape raspberries strawberries turnips vegetables wheat	
Portugal	commercial	almonds apple beans broad beans cabbage carrots grapes hops maize/corn onion ornamental plants garden peas peaches pears plums strawberries tomatoes	E 605 forte 500 g/l EC Reg No: 1875 E 605 PO 20 g/kg WP Reg No: 1813
Spain	commercial	cotton ornamental plants pome fruit stone fruit	Folidol 20 PM 20 g/kg Reg No: 15769
		grapes pome fruit stone fruit	Oleo Folidol 3 690 g/l EC Reg No: 13578
		grapes pome fruit stone fruit	Oleo Folidol 5 LE 580 g/l EC Reg No: 12882

LEVEL 2

Parathion

Reasoned statement of the overall conclusions drawn by the Rapporteur Member State

2.1 Identity

Parathion (ISO common name) is an organophosphorus compound. There are no structural isomers.
Ethyl parathion EC 100 is an emulsifiable concentrate containing 100 g of parathion per litre. Ethyl parathion EC 500 is an emulsifiable concentrate containing 500 g parathion per litre.
The biological mode of action of parathion is by an indirect cholinesterase inhibition.

2.2 Physical and chemical properties

Parathion has limited water solubility and is degraded by hydrolysis and photolysis. No adsorption above 290 nm in UV spectra. Its log K_{OW} of approximately 3 indicates a potential for bioaccumulation. The flammability, explosive or oxidising properties are not critical.

Parathion formulations are not explosive, not oxidising and their pH are within naturally occurring ranges, e.g. in soil. The technical properties indicate that no particular problems are to be expected when used as recommended. The flashpoint of 31°C of ethyl parathion 500 EC classifies this formulation as a flammable liquid.

2.3 Details of uses and further information

Parathion is an insecticide, acting by contact and ingestion. The target organ within the pest is the nervous system. Pest controlled are mostly biting and sucking insects.
Parathion is not systemic in plants. Parathion is used as a spray treatment in agriculture, horticulture, forestry and viticulture.
It provides a broad spectrum of activity at rates of use of 150 - 600 g a.i./ha.

Both parathion formulations are packed in 1 litre HDPE bottles and 5 litre HDPE containers, which have been tested and are considered acceptable to ADR standards.

For information on handling, storage, transport and fire, a safety data sheet is available.

2.4 Impact on human and animal health

2.4.1 Effects having relevance to human and animal health arising from exposure to the active substance or to its transformation products

Absorption, distribution, excretion and metabolism

The studies on rats showed a high degree of absorption followed by fast elimination from the body. Thus, 99% of an oral or intravenous [^{14}C] dose was excreted in urine and faeces within 2 days. The

primary route of elimination was via the urine, 86-94% of the administered radioactivity after oral dosing, and 99% after i.v. injection, whereas the elimination via the faeces was 6-13% following the oral dose.

Only 0.2% of the orally administered radioactivity was distributed in the animals after 48 hours, levels in tissues such as liver, kidney and fat and blood plasma being low. Less than 0.07% of the oral dose was eliminated in expired air after 24 hours. These results were independent of dose level.

Other species exhibited a similar rapid absorption and elimination of parathion.

Oral administration of [^{14}C] parathion to mice at a dose of 1 mg/kg resulted in elimination of 17% of the dose in urine and 3.7% in expired $^{14}CO_2$ after 1 hour. Distribution in [^{32}P] studies in mice indicated that after 30 minutes highest levels were in cervical brown fat and salivary glands, whilst activity in the bladder and adipose tissue increased gradually over a period of 4 hours.

In dogs, sequential intravenous and oral [^{14}C] doses, with an interval of one week between doses, were rapidly excreted via the urine, and activity was distributed to a wide range of tissues.

Intravenous administration of [^{14}C] parathion to rhesus monkeys indicated that 54-75% of the radioactivity was eliminated via the urine in 24 hours.

Percutaneous administration of parathion to the abdomen of rhesus monkeys for 14 days, the first and eighth applications being radiolabelled, indicated that 40% of the administered radioactivity passed through the skin after either of the labelled doses, a maximum rate of 0.4-0.5% of the dose per hour was excreted in the urine being reached after 50 hours after dosing.

After administration of 97 mg/kg in the diet on five consecutive days, to lactating goats, total radioactive residues in tissues, organs and milk were relatively low. Highest levels of radioactivity were in liver, kidney, renal fat and muscle.

After administration of 16.5 mg/kg in the diet on six consecutive days to laying hens, the highest radioactive residue concentrations were found in liver, kidney and skin fat, although these were of a very low percentage of the dose. The concentration of radioactivity in eggs ranged from 0.003-0.015 mg parathion equivalents/kg.

In studies on the intravenous administration of [^{14}C] parathion to piglets, urinary excretion rose from 18% for new born piglets to 82% of the dose for eight-week old piglets during the first 3 hours.

The excretion of radioactivity from pigs was 29-49% 168 hours after a dermal application of [^{14}C] parathion under occluded conditions. When applied unoccluded, excretion of radioactivity was much lower at 8-25%, mostly in the urine.

In metabolism studies, the major urinary metabolite found after oral or intravenous administration of [^{32}P] or [^{35}S] parathion to male rats was O, O-diethyl phosphorothioate.

Other products, resulting from the degradation of the active metabolite paraoxon, were diethyl phosphate, p-nitrophenol and desethyl paraoxon. In adult rats, paraoxon is more slowly metabolised by females than males, resulting in enhanced toxicity.

When mouse livers were perfused with parathion, the metabolites, paraoxon and p-nitrophenol and its glucuronide and sulphate conjugates appeared in the effluent, and p-nitrophenol was identified in the urine of rabbits.

In an early study, neither parathion nor p-nitrophenol were detected in the blood or milk of five cows which were fed parathion in their feed for 61 days.

In lactating goats, [^{14}C] studies indicated that the major metabolite in milk, liver, kidney, renal fat and muscle (19-40% of radioactivity residues in tissue) was O, O-diethyl p-(acetemidophenyl)phosphate, with parathion being a minor constituent (2.5-16%). p-Acetamidophenol was also an abundant metabolite in liver and kidney, and small amounts of p-aminoparathion and p-nitrophenol were found in some tissues.

In laying hens, [^{14}C] studies suggested that the major metabolite was p-acetamidophenol in eggs, liver, kidney and skin/fat (11-25% of residue in matrix). Parathion was a minor constituent (<2%) in tissues, and in eggs (< 5%).

Small amounts of p-aminophenol were found in eggs and paraoxon and p-acetamido-paraoxon were found in liver and kidney. Other metabolites identified in eggs and tissues were p-nitrophenol, p-acetamidophenol, p-nitrophenylsulphate and O-ethyl-p-nitrophenylphosphorothioate.

In piglets, the main metabolites in plasma and tissues in plasma and tissue were p-nitrophenol and its conjugates.

The overall metabolic pathways are similar in all mammalian species studied, although degradation processes are somewhat different in ruminants and hens.

Parathion undergoes oxidative activation (desulphurisation) by mixed function oxidases to the toxic agent paraoxon, which has not been detected in metabolism studies. The principal site of metabolism is in the liver, although other tissues such as lung and skin may be involved. The toxicity of parathion is influenced by the comparative rates at which it and paraoxon are broken down. Both parathion and

paraoxon may split (hydrolyse) to give diethyl thiophosphate (or diethylphosphate from paraoxon) and p-nitrophenol, involving carboxyesterases.

De-ethylation to desethyl compounds is an important metabolic pathway, possibly catalysed by hepatic oxidases and glutathione-linked reactions.

Parallel reactions take place for paraoxon and lead to detoxification.

Ruminants and hens appear to have an additional major pathway involving reduction of the nitro group to give aminoparathion and further related products by reactions such as N-acetylation and glucuronide and sulphate conjugation.

Mammalian toxicity

Parathion is classified, by reason of its chemical structure, as an ester of thiophosphoric acid. It may be converted *in vivo* to the active metabolite, paraoxon, which acts as an acetylcholinesterase inhibitor, causing accumulation of acetylcholine at nerve endings in the peripheral or central nervous system.

Parathion is highly toxic on acute oral administration to rats, especially females, because they are less capable of detoxifying parathion by the mechanisms described in the metabolism section. This sex difference is not evident in other species. Examples of clinical signs include ataxia, tremors, hypopnea, salivation, lacrimation and hypoactivity.

Recovery from toxic effects in surviving animals is also rapid, usually within a few days. Mice, guinea-pigs, rabbits, cats, dogs and sheep appear to have the same level of sensitivity as male rats.

Parathion is highly toxic to rats, mice and guinea-pigs after intraperitoneal administration, emphasising the rapid absorption following oral administration Studies in rats demonstrated greater toxicity for weanlings because of a less developed detoxification mechanism than the adults.

The toxicity of parathion is high when applied dermally to rats, but it has relatively low dermal toxicity to rabbits. Signs of toxicity in affected rats included ataxia, tremors, hypoactivity, salivation, prostration and hypopnea.

Parathion is also toxic to rats via the inhalation route.

Parathion is neither a skin irritant nor an eye irritant, only transient effects being observed. No evidence of a skin sensitisation potential was found.

Ethyl parathion 500 EC formulations have high acute oral toxicity, moderately high acute dermal toxicity and high acute inhalation toxicity. The skin and eye irritant properties of the EC formulations are taken into account in the context of the recommendations for their use.

Table 2.4.1-1: Summary of the results of acute toxicity testing

Test	Parathion	Formulations
Oral, Rat	2 (f) 22 (m) mg/kg b.w.	500 EC 5 - 20/> 1 - 9 mg/kg b.w. (m/f)
Oral, mouse	6.0 - 25.0 mg/kg b.w.	---
Oral, guinea-pig	9.3 - 32.0 mg/kg b.w.	---
Oral, rabbit	40.0 mg/kg b.w.	---
Oral, dog	8.3 mg/kg b.w.	---
Dermal, rat	71 - 100 mg/kg bw 6.8 - 24.0 mg/kg.bw (not removed)	500 EC 139/134 mg/kg b.w. (m/f)
Dermal, rabbit	910 - 1400 mg/kg b.w.	500 EC 219 - 340 mg/kg b.w.(m/f)
Inhalation, rat, 1hr	71 - 245 mg/m^3	---
Inhalation, rat, 4hr	30 - 94 mg/m^3	500 EC 82/50 mg/m^3 (m/f) 61 mg/m^3 (m/f)
Skin irritation, rabbit	not irritant	500 EC Undiluted: slightly irritant to irritant 0.1% dilution in water: not irritant
Eye irritation, rabbit	not irritant	500 EC Undiluted: irritant 0.1% dilution in water: not irritant
Skin sensitisation	not sensitising	not sensitising

Table 2.4.1-2: A concise summary of the results of short-term toxicity, long-term toxicity, and neurotoxicity testing

Type Of Study	Test Species	Result Obtained With Most Sensitive Test Species
Oral, 14 days	rat	NOEL: 1mg/kg in the diet, erythrocyte cholinesterase inhibition seen at 5 mg/kg.
Oral, 90 days	rat	NOEL: not found due to inhibition of erythrocyte at the lower dose 0.5 mg/kg.
	dog	NOEL: 0.3 mg/kg b.w. for m, not established for f.
Dermal, 15 x 6 h/day	rabbit	NOEL: 0.1 mg/kg bw, inhibition of erythrocyte, plasma and brain cholinesterase activity at 2 mg/kg.
Inhalation, 15 x 6 h/day	rat	NOEL: 0.25 mg/m^3 air,
Inhalation, 30 x 7 h/day	rat	LOEL: 0.0 1 mg/m^3 air, inhibition of erythrocyte cholinesterase .
Oral 6 months to asses ocular lesions	dog	NOEL: 0.079 mg/kg b.w., plasma, erythrocyte and retinal cholinesterase inhibition.
Oral, 12 months	dog	LOEL: 0.01 mg/kg in the diet, cholinesterase inhibition at 0.03 mg/kg.
Oral, 2 years	rat	first study. NOEL: 0.025 mg/kg/day. second study NOEL 0.1 mg/kg for inhibition of ChE, 0.4 mg/kg for retinal atrophy
Neurotoxicity, oral	hen	Negative
Neurotoxicity, subcutaneous	hen	Negative

In short-term (14 day, 6 x 5 days/week, 90 day) studies in rats using oral administration, inhibition of erythrocyte, plasma cholinesterase and in the longer studies, brain cholinesterase activities, were observed at the higher doses.

In 90-day studies, high dose effects included mortalities, toxic clinical signs, reduced weight gain, decreased body weight, reduced red cell count, effects on several biochemical parameters and reduced organ weights. Typically females were affected more than males. Plasma and especially erythrocyte cholinesterase inhibition was observed at intermediate doses.

Only reduction in body weight gain at the top dose was observed in a 90-day oral study on mice, whilst in short-term oral (6 x 5 days/week, 9 weeks, 90 days and 6 months) studies in dogs, plasma

and erythrocyte cholinesterase inhibition was observed at high and intermediate doses, and although retinal cholinesterase inhibition was noted at the top dose in one study, no functional or morphological changes to the eyes were seen.

In a 9-week study, plasma cholinesterase activity returned to normal after 4 weeks on a control diet. Other parameters affected at high dose were reduction in body weight, decrease in serum albumen and increase in ß-globulin. Retinal cholinesterase activity was decreased in top dose animals, but no functional or morphological changes to the eye were noted.

The only significant effect observed in a short-term dermal toxicity study in rabbits was inhibition of plasma, erythrocyte and brain cholinesterase at the top dose. Short-term inhalation studies in rats and dogs also indicated inhibition of cholinesterase activity, the sensitivity tending to increase in the order brain < plasma < erythrocyte, so that effects on plasma and erythrocyte levels tended to be detected at intermediate levels, whilst the brain cholinesterase effects tended to be detected at high levels. Mortalities, lung congestion and clinical signs of toxicity were seen in rats given a high dose level, particularly females.

The overall evidence provided by genotoxicity studies on parathion is lack of significant mutagenic/genotoxic activity. *In vitro* tests in bacteria, yeast and mammalian systems mainly provided negative findings.
The results of two *in vitro* studies which indicated weak positive results were not confirmed in subsequent studies. Furthermore, parathion did not exhibit mutagenic activity in the *in vivo* mouse bone marrow micronucleus or dominant lethal assays.

Parathion showed no evidence for carcinogenic potential in two long-term rat studies. In a mouse study, an increased incidence of alveolar/bronchiolar adenomas at the lowest dose levels in males and in malignant lymphomas in females, was not considered to be related to treatment, as incidence of these tumours was within contemporary and/or historical control incidences. This indicates that parathion is not carcinogenic when fed continuously long-term to the mouse in studies.

Several studies have been undertaken involving longer-term administration (1 and 2 years) in rats, mice and dogs. At the highest dose levels, the toxic effects were those expected from the compound, namely increased mortality in some cases, reduced body weight gain, cholinergic and clinical signs, peripheral neuropathy and reduced red cell count. At these levels, cholinesterase activity in erythrocytes, plasma and brain were all markedly inhibited.

Retinal degeneration was noted at high doses only in the rat, and this effect appears to be an enhancement of the normal degenerative processes seen in the eyes of ageing control animals.

Reduction of retinal cholinesterase activity was observed at high dose levels in the dog. However, in this study there were no associated morphological changes in the retina.

Two-generation studies in rats indicated that, at high doses adults in both generations exhibited tremors whereas a decrease in body weight gain was observed in F0 and F1 adults in one pre-GLP study even at the lower dose level tested, 5 ppm. In the more recent and adequate study the NOEL for parental toxicity was 1 ppm in the diet, equivalent to 0.05 mg/kg b.w. No effects were observed on parameters of reproductive performance, i.e. mating, gestation, fertility indices; in both studies, F_1 pup body weight at birth and survival were decreased (LOEL and NOEL 20 and 10 ppm). Cholinesterase activity was measuered in one study in adults only. In both generations brain cholinesterase activity was reduced at 20 ppm in females only, whereas plasma cholinesterase activity was inhibited at $\geq$ 10 ppm (NOEL 5 ppm). No data are available on cholinesterase inhibition in pups.

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In the oral teratogenicity studies in rats and rabbits, mortalities were observed among the top dose dams. Reduction in body weight gain with other clinical signs of toxicity and low placental weights were seen in rats which were more sensitive than rabbits. In fact clinical signs were observed in rats in one study even at the lower dose level tested, 0.25 mg/kg b.w. There was no overall increase in malformations in foetuses; increased resorption rate was observed in one out of two rabbit studies (LOEL and NOEL 0.3 and 0.1 mg/kg b.w.).
In a rat dermal study, using one dose level, significantly decreased implantation rate and increased embryonic death were observed.

No data are available concerning the potential of parathion for inducing developmental neurotoxicity following peri-postnatal exposure.

Table 2.4.1-3: A concise summary of the results genotoxicity, carcinogenicity, reproductive toxicity, and teratogenicity

Type Of Study	Test Species	Result Obtained With Most Sensitive Test Species
Genotoxicity/ mutagenicity in vitro	Bacteria, yeast, mammalian cells	Not mutagenic and/or genotoxic
Mutagenicity in vivo	mouse b.m. micronucleus, dominant lethals	not mutagenic
Carcinogenicity/ Oncogenicity	rat	NOEL: 50 mg/kg in the diet (maximum dose = 50 mg/kg)
	mouse	NOEL: 60 mg/kg in the diet ,tumours found at 100 mg/kg.
2-generation	rat	NOEL: 1.25 mg/kg bw, the maximum dose.
Teratogenicity, oral	rat	NOEL: 1.5 mg/kg bw[xx], the maximum dose.
	rabbit	NOEL: 16 mg/kg/day, the maximum dose.

xx no teratogenic or embryotoxic effects, but maternal toxicity

Atropine and oxime reactivator compounds, such as Toxogonin, are well known antidotes to parathion poisoning. Use and effectiveness of these antidotes in cases of human poisoning are well documented in the scientific literature.

In mechanistic studies on guinea-pigs, it was demonstrated that plasma, brain and cholinesterase activities are inhibited rapidly by oral or intraperitoneal dosing. These effects are readily reversible with levels returning to normal within seven days.. Oral studies in rats indicated that there was no relationship between blood cholinesterase depression and electroretinogram (ERG) abnormalities on this basis, and there was no effect on basal lung resistance.

In a study on enzyme systems, parathion was shown to inhibit human non-specific esterases more strongly than acetylcholinesterase, and was a weak inhibitor of microsomal enzyme systems, O-demethylase, O-dearylase, N-demethylase, azoreductase and nitro-reductase in rat liver preparations.

Typically, parathion has shown only additive or sub-additive (antagonistic) effects when simultaneously administered with other pesticides by oral or intraperitoneal dosing in laboratory

animals. Examples tested have been other organophosphorus compounds, such as dimethoate, disulfoton and trichlorfon. However, trichlorfon has been reported to cause a potentiating effect.

Some compounds which can accelerate the rate of metabolic breakdown by hepatic enzyme induction (eg phenobarbitone) may decrease acute toxicity.

Controlled investigations with human volunteers over several weeks have shown that parathion, given orally, may inhibit plasma and erythrocyte cholinesterase activity and some of these studies indicated levels at which parathion did not affect this sensitive indicator.

2.4.2 Acceptable daily intake (ADI)

Following use of preparations containing parathion, a consumer risk, in terms of organ toxicity, genotoxicity and reproductive toxicity does not arise. There is no evidence of bioaccumulation.

The calculation of an acceptable daily intake is based on the results of the chronic feeding studies in the rat, mouse, dog and human volunteer investigations. The following no-observed-effect levels (NOELs) were found in these studies:

Rat	chronic feeding study 2 ppm, equivalent to 0.1 mg/kg body weight/day, based on plasma and erythrocyte cholinesterase inhibition activity, brain cholinesterase inhibited at 1.6 mg/kg body weight/day.
Dog	chronic feeding study 0.01 mg/kg body weight/day, based on plasma and erythrocyte cholinesterase inhibition activity, no significant changes in brain cholinesterase activity.
Human Volunteers	0.06 mg/kg body weight/day, based on slight inhibition of plasma cholinesterase activity at a dose level of 0.08 mg/kg/day.

The proposed acceptable daily intake is established on the basis of the highest dose at which no adverse effect is observed. The most relevant toxicological information is derived from the controlled studies in humans. By monitoring blood cholinesterase activity, the most sensitive indication of exposure, the outcome of several volunteer studies is that no biological significant changes occur at dose levels of 0.06 mg/kg bw/day based on a slight inhibition of blood cholinesterase. Even at doses of 0.08 mg/kg/day only slight effects on plasma cholinesterase were seen.

This human evaluation is supported by the results from the numerous shorter and longer-term animal studies. At the highest dose levels in these studies, blood (plasma and erythrocyte) cholinesterase inhibition is often accompanied by general toxic effects of the compound.

At lower dose levels, where the other effects are not evident, measurement of blood cholinesterase activity provides the most sensitive indication of exposure.

On this basis, 'no effect' levels were established in long-term studies of 0.1 mg/kg bw/day in rat and 0.01 mg/kg bw/day in the dog.

With a clear 'no effect' level established in man, based upon the most sensitive parameter, allows a 10-fold safety factor for the calculation of the ADI. This gives a value of 0.006 mg parathion/kg body weight.

In 1967, an ADI of 0.005 mg/kg body weight was agreed on the basis of an evaluation of parathion by the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (WHO, 1967). This still seems to be a justifiable value in view of further evidence since that time. In 1995 the ADI was re-evaluated and a value of 0.004 mg/kg body weight was agreed.

2.4.3 Acceptable operator exposure level (AOEL)

The NOEL of 0.06 mg/kg b.w. determined in human volunteer studies is used to calculate the AOEL.

Since the NOEL has been derived from toxicity tests in humans, a 2.5-fold Safety Factor would be suitable to account for intraspecies variability. However, in light of the fact that this NOEL is based on an acute end-point (cholinesterase inhibition), the Safety Factor should be increased to at least a factor of 10, in order to have a margin of safety high enough to protect against the onset of acute effects. A higher Safety Factor is also necessary when considering that the human studies from which the NOEL was derived had been performed at times when analytical methods for cholinesterase determination were rather poor.

On this basis, the Acceptable Operator Exposure Level is 0.006 mg/kg/day.

2.4.4 Drinking water limit

Field studies demonstrated that parathion is not mobile below a 10 cm soil depth, indicating that under normal agricultural use there is no potential risk of contaminating drinking water supplies. However, the method for determining parathion residues in water is sensitive enough to satisfy the EC Directive relating to the quality of water intended for human consumption 80/778/EEC of 15 July 1980. In which the concentration of any one pesticide must not exceed 0.1 µg/l.

On the basis that exposure through drinking water should not account for more than 10% of ADI, assuming average consumption of 2 litres of water per person per day and body weight of 60 kg, a limit of 18 µg/l is proposed.

2.4.5 Impact on human or animal health arising from exposure to the active substance or to impurities contained in it

Parathion's toxicology has been evaluated in a wide range of studies over many years and there is a good understanding of its mode of action. The critical effect is inhibition of cholinesterase activity. The compound is converted into its more active metabolite, paraoxon-ethyl, which inhibits cholinesterase activity at nerve endings and produces the resultant toxic action.

Cases of poisoning have been reported over the life of the compound. The symptoms of parathion poisoning are weakness, nausea, vomiting, excessive sweating, headache, tightness in the chest, laboured breathing, sweating, excessive salivation, difficulty in walking, miosis, muscle fasciculation and coma.

No data on medical surveillance of manufacturing plant personnel are reported in the dossier. Comprehensive information is missing concerning results on biological monitoring of workers, cases of acute poisonings, epidemiological results on the occupational or general population. Further information on these issues has been required, since the lack of these data is not acceptable for a product which has been used for many years,.

The risk of systemic effects arising from operator exposure to the active substance during mixing and application activities has been estimated for Ethylparathion EC 500. Ethylparathion EC 500 is a broad-spectrum insecticide used on a variety of crops including vegetables, fruit trees, field crops, protected crops and ornamental plants. It is applied using field crop sprayers, portable or hand-held sprayers and air assisted fruit-tree sprayers.

Operator exposure estimates, calculated using the experimentally determined specific exposures provided by the German Generic Database (Lundhen et al., 1992) indicate that, when no personal protective equipment (PPE) is worn, the AOEL will be exceeded in all scenarios of exposure, whether assuming a 20% or a 10% skin absorption,.

When traditional personal protective equipment is worn, the AOEL will still be exceeded in two exposure scenarios: tractor-mounted and hand-held applications in high crops.

Therefore, the margins of safety obtained by calculation are inadequate, and the risk is not acceptable.

The results of risk evaluation based on Generic Databases to predict operator exposure indicate the need to proceed to a Tier-III risk assessment, based on actual measurements of exposure, rather than on exposure estimates.

Furthermore are completely lacking informations on the result of health workers surveillance, nevertheless the compound was widely used in the past.

2.5 Methods of analysis

2.5.1 Analytical methods for analysis of the active substance as manufactured

The analytical method for the determination of parathion as manufactured and in plant protection products is the same. It is satisfactory in terms of peak resolution, column efficiency and linearity of detection. The assay accuracy in the calibration range is good with a correlation coefficient of the calibration curve of 0.99997. The method satisfies the requirements of the Directive 96/46/CE (16 July 1996)

2.5.2 Analytical methods for formulation analysis

See 2.5.1.

2.5.3 Analytical methods for residue analysis

Due to the lengthy working life of parathion and its formulations the available analytical methods for the determination of parathion residues in food and feeds are relatively old, ranging from 1974 to 1982. The confirmatory methods of analysis range from 1948 to 1978. It is evident however, that none of the methods available completely satisfy the requirements of the Directive 96/46/CE (16 July 1996)

The substance is usually analysed by gas chromatography (GC) with various detectors: alkali flame ionisation detector (AFID); trace flame photometric detector (FPD); electron capture detector (ECD); phosphorus flame ionisation detector (phosphorus FID); thermionic selective detector (TSD). Water samples are analysed by thin layer chromatography (TLC) with UV/visible detection. Animal and human body fluids and tissues may be analysed by GC/FPD or GC/ECD or thermionic detection of ammonium molybdate/ascorbic acid treated samples following oxidation.

Limit of determination (depending on particular method used):

in plants, plant products, foodstuffs, feedingstuffs:	0.02 mg/kg
in soil:	0.01 mg/kg - 0.1 mg/kg
in water:	0.05 µg/l
in air:	0.0046 mg a.i./m^3
in animal and human body fluids:	1 ng

2.6 Definition of the residues

2.6.1 Definition of the residues relevant to MRLs

The studies on the metabolism of [^{14}C] parathion demonstrate that, after application to plants, there was little evidence of translocation from foliage. Residues in potato tubers and cotton seeds were low at 0.12 mg/kg and 0.04 mg parathion equivalents/kg, respectively, after high application rates. In wheat grain, following unrealistically high levels of application, 8.5 mg parathion equivalents/kg were found, but much less radioactivity penetrated to the wheat grain than to the foliage or the chaff.

In cotton and potato, the amount of non-extractable residues was higher in seed and tubers, respectively, than in foliage, whilst in wheat, non-extractable residues declined in the order straw > chaff > grain.

In all three crops, the parent compound was the major component of the radioactive residue. Identified metabolites were p-nitrophenol, p-nitrophenylglucopyranoside, paraoxon, S-phenylparathion, S-ethylparathion, O-ethyl-p-nitrophenyl phosphorothioate, p-nitrophenylphosphate, and p-aminoparathion. All these metabolites were present at below 10% of the applied radioactivity. Consequently the parent compound has to be regarded as the only residue of concern.

The main uses of parathion are in perennial crops where rotation is not important.

Metabolism studies on rats showed a high degree of absorption of the radioactivity followed by fast elimination from the body. Thus, 99% of the orally administered dose had been excreted after 2 days.

In metabolism studies most of the radioactivity eliminated in the urine could be identified. The predominant urinary metabolites were O, O-diethylphosphorothioate and diethyl phosphate from [^{32}P] parathion studies, and p-nitrophenol and ethyl paraoxon from [^{14}C] compound studies. In lactating goats, the major metabolites were O, O-diethyl(p-acetamidophenyl)phosphate, p-acetamidophenol, p-aminoparathion and p-nitrophenol.

In laying hens, the principal metabolite was p-acetamidophenol, which was found in eggs, liver, kidney and skin fat. Small amounts of parent compound were found in tissues and eggs.

Although metabolites in different animal species differ to some extent, the basic metabolic steps are the same. Some additional reductive pathways are found in ruminants and hens.

The radiolabelled studies on lactating goats indicated that feed consumption, milk production and body weights were not affected by daily oral administration of 188 mg/goat/day for five days.

The uses of parathion mean that it is unlikely that treated crops will be used in animal feed, except in the case of maize fodder crops. Although residues of parathion were found in maize fodder, the application rates and number of applications used in the trials were 5-10 times greater, and the PHIs were shorter. Hence the residues of parathion in animal feed containing maize fodder are likely to be very low.

No differences were seen between the parathion-treated group and the control group of laying hens with respect to feed consumption. The uses of parathion mean that it is unlikely that treated crops will be used in animal feed, except in the case of maize fodder crops and apple pomace. Although residues of parathion were found in maize fodder, the application rates and number of applications used in the trials were 5 - 10 times greater, and the PHIs were shorter. Hence the residues of parathion in animal feed containing maize fodder are likely to be very low. No significant residues were found in apple pomace under conditions reflecting the proposed application rates and number of applications.

GC/FID and GC/ECD methods to determine parathion residues in plant materials are available. The recoveries were 55 - 130% and the limits of determination were 0.02 - 0.1 mg/kg.

As no metabolites in plants exceeded 10% of the total radioactive residue, and all main metabolites were also identified in animals, the parent compound has to be regarded as the only residue of concern.

2.6.2 Definition of the residues relevant to the environment

As parathion is rapidly degraded in soil, water and air, the parent compound is the only substance of concern for the environment.

2.7 Residues

2.7.1 Residues relevant to consumer safety

To clarify the residue behaviour of parathion, numerous residue trials were conducted on different crops (for details see MRL proposals) to support the registered uses of 500 EC, 570 EC, 960 EC, 175 EC, 160 EC, 800 EC and 250 WP formulations in Northern and Southern European countries. The results show that the residues declined with time are independent of the type of formulation.

Freezer storage stability studies indicated that parathion is stable in a variety of crops for up to 24 months.

The effect of processing was investigated on apple (unclarified) juice, apple wet and dry pomace, cider and vinegar, orange juice, wet and dry pulp, C.P. oil and molasses, lemon dried peel, wet peel,

juice, C.P. oil and molasses, grapefruit wet and dry pulp, juice, oil and molasses, grape juice, raisins, raisin waste, wet and dry pomace, wine, must, sediment, maize flour, grits, meal, starch, crude and refined oil, wheat bran, flour, middlings, shorts, chaff and grain dust.

In general, the results indicated that parathion and paraoxon tended to be concentrated in fruit pomace, peel and C.P. oil and in maize, in crude and refined oil, but the commodities used in the experiments had been treated with application rates and number of applications well above those recommended in the registered uses. Parathion residues in cider, apple vinegar (from dosing studies) and wine were reduced by sorption onto sedimented matter, and in the case of wine by hydrolysis to p-nitrophenol. In cider and apple vinegar, aminoparathion residues decreased during storage.

In wine, levels of the two metabolites, paraoxon and aminoparathion were low in both the wine and the lees, indicating that oxidation and reduction were not significant. Parathion residues declined under all storage temperatures, whereas paraoxon and aminoparathion levels were unaffected by storage.

Due to the lack of data for the intended uses, no residue definition for risk assessment can be recommended, no potential dietary exposure can be estimated.

2.7.2 Residues relevant to worker safety

Parathion formulations are normally used at times when entering the crops shortly after spraying is not necessary. The half-life of the active ingredient in air is less than 1 day.

2.7.3 Compliance with existing MRLs and/or proposed MRLs

In January 1998, Cheminova and Bayer have been submitted a list of crops they intend to support.

The residue results of parathion in the crops supported are listed below:

Commodity	MRL proposals (mg/kg)
Pomefruit	0.2
Peach, stone fruit	1.0
Citrus	1.0
Grapes	2.0

2.8 Fate and behaviour in the environment

2.8.1 Fate and behaviour in soil

2.8.1.1 Route of degradation

The dissipation of parathion in soil is mainly due to photolytic processes and microbial degradation.

At the end of a 12 months aerobic study, a cumulative percentage of 43% of CO2 was noticed. Besides $^{14}CO_2$ which was the principal aerobic degradation product, other metabolites like p-nitrophenol, paraoxon and O, O-bis(4-nitrophenyl)ethylphosphate which were detected at levels each less than 5%.

Significant amounts of non-extractable radioactive residues were formed which reached their maximum of 49.1% of the initial dose after 92 days of incubation and then fell slowly to 36.6% after 366 days.

In another laboratory study , in which two different soils were used, after 135 days of incubation at 22°C, 35-40% of the applied parathion was mineralized to CO2.

No data from studies of anaerobic degradation in soil are available.

Soil photolysis studies showed that after 28 days parathion gave rise to the formation of paraoxon (4.6%), 4-nitrophenol (7.5%), and unknown products (3%).

2.8.1.2 Rate of degradation

The rate of degradation due to chemical/microbial processes in a laboratory study was such that DT_{50} value was of 57,1 days at a temperature of 25°C. This value was substancially confirmed in another laboratory study conducted at 28°C, using two soils. The DT_{50} from laboratory soil photolysis studies is 73 days, compared to a DT50 of 182 days for the dark control.

Two in field dissipation studies were conducted in two sites in the USA, on three replicate plots of cotton treated with six applications at a rate of 1.1 Kg/ha. The temperatures during the study were in the interval of 19-35°C in the loam soil and 19-36°C in the sandy loam soil. The humidities were of 83-90 and 19-92%, respectively . From the concentrations of parathion determined in the 0-10 cm layer , DT_{50} values of 3 and 32 days were obtained in the sandy loam and in the loam soil, respectively.

In another in field study conducted in two sites in Germany, 350 g a.i./ha were applied on plots of silt loam and sandy loam soils. DT50 values from these studies calculated from the concentrations in the 0-10 cm layer of soil were within the interval of 5-19 days.

The results from these studies show that parathion does not accumulates in the soil and its uptake by following crops is not expected.

No studies on the degradation in the saturated zone have been conducted as it is unlikely that parathion reaches this zone.

2.8.1.3 Adsorption and desorption

Four soils were treated at nominal concentrations from 0.12 to 4.0 ug/cm3 of a.i. Kd and Koc values were of 1.71-25.28 and 1133-1710, respectively.

The results from these studies show that parathion has a low mobility in the soil as is confirmed by field trials which have demonstrated that detectable residues were only present in the top 10 cm of soil.

2.8.1.4 Mobility in soil

The mobility of parathion is expressed by the above mentioned studies. Its Kd and Koc values in four different soil as well as the in field studies show that this compound has a low mobility in soil.

2.8.1.4.1 Aged residue column leaching

The results from a study conducted using two soils showed that ,after ageing, the proportions of the originally applied radioactivity eluted from the soil columns amounted to 0.23 and 0.28% in the two soils.

The conclusion from this study is that parathion and its degradation products have a very low leaching potential.

2.8.1.5 PECs in soil

The notifier has calculated the PECs in soil for the main uses and rates of application of the a.i., as summarised in the table 2.8.1.4.

Table 2.8.1.4: Predicted Environmental Concentration (PEC) in soil.

Crop	**Soil coverage**	**Typical Application rate (a.i.)**		**Portion of a.i. reaching the soil**		**PEC_i (mg a.i./kg d.wt. soil)[a]) related to 5 cm soil depth**
		kg/ha	**mg/m^2**	**kg/ha**	**mg/m^2**	
Field crops	50%	0.2	20	0.1	10	0.13
Orchards Vines	50%	0.3	30	0.15	15	0.2

[a]) d. wt. = dry weight

Based on a typical application rate, the highest predicted concentration in soil is estimated to be 0.2 mg/kg dry weight. Prolonged exposure is not expected.

2.8.2 Fate and behaviour in water

2.8.2.1 Route and rate of degradation

Chemical hydrolysis.

The hydrolysis of parathion was investigated at 25°C , at pH 5 and 7. There was very little hydrolysis with respective half-lives of 133 and 247—356 days (depending on the buffer solution). In alkaline conditions the half life was reduced to 102 days. Similar results were obtained in other studies, from which p-nitrophenol and diethyl thiophosphate (diethyl thiophosphoric acid) were identified as degradation products in trace amounts.

Biological hydrolysis

The degradation of parathion was investigated in sterile and non-sterile river water at about 28°C. The experiments were conducted at pH 8.2 (that of the water) and 6 and 7(amended). The half-lives varied between 30.8 and 46.5 days under sterile conditions and were reduced to 7.8-12.6 days in non-sterile samples .

Photochemical degradation

Half-lives of parathion of 203, 30 and 4.4 days were obtained for dark controls, non-sensitised samples and samples sensitised with acetone (1% v/v), respectively. After 30 days from the beginning of the experiment, 12.8% of the radioactivity was mineralized to CO2 in the non-sensitised sample respect to 14.6% in the sensitised sample. In the non-sensitised sample, in addition to the parent compound which accounted for 51.0% , 8.4% 4-nitrophenol, 3.4% paraoxon and 2.3% S-phenyl parathion and/or S-ethyl parathion were found. The unknowns were tentatively identified as 14.2% hydroquinone and 5-6% 4-nitrophenol. One unknown fraction of 5-6% could not be identified.
In a study on the influence of humic acid on the photolytic breakdown of parathion, it was observed that addition of 500 mg/l of humic acid decreased the half-life of parathion by a factor of about 17, from 39 to 2.3 hours.

2.8.2.2 Ready biodegradability

Not performed

2.8.2.3 Water/sediment study

The degradation of parathion was studied in two microecosystems whose water and sediment samples were collected from a ditch and a small lake. After 14 days parathion could not longer be detected in the surface water of the ditch system and a maximum of 1.4% of the applied dose was present in the

sediment. In the lake systems up to 24% of the applied parathion was found in the surface water and up to 13% in the sediment.Parathion was metabolized to aminoparathion, which then decreased gradually in the water. Mineralization of parathion to 14 CO2 was negligible.

In another study, in which samples of soil and water were placed in sealed bottles and incubated for in the dark for 31 days, a half-life of 5.2 days was calculated for parathion. Volatiles amounted to 3% of the initial dose, mainly as CO2. Non-extractable residues in the soil increased steadily to a maximum of 60% of the applied radioactivity at the end of the study. These residues were partly due to parathion. The principle metabolite was 4-nitrophenol which reached a maximum level of 27% of the applied radioactivity within 7 days, then declined to 12% at the end of the study. Paraoxon and O, O-bis(4-nitrophenyl)ethylphosphate were found in trace amounts.

2.8.2.4 Field paddy study

In field studies on paddy rice, the aquatic dissipation of parathion was so rapid that a half-life could not be determined. No residues of parathion and paraoxon were detected in soil (or plant) samples, and in the water neither paraoxon nor p-nitrophenol were detected.

2.8.2.5 PECs in ground and surface waters

The very low mobility of parathion and PELMO modelling calculations on the closely related compound parathion-methyl indicate that parathion residues are not expected to reach ground water.

PECs in surface waters following the main uses and rates are reported in table 2.8.1.5.

Table 2.8.1.5: PEC_i (initial) in water, ground application

Crop	**Distance**	**Drift**	**Application rate (a.i.)**		**Portion of drift (a.i.)**		**PEC_i (µg a.i./l, ppb) 1m water depth**
	(m)	**(%)**	**kg/ha**	**mg/m^2**	**kg/ha**	**mg/m^2**	
Arable crops	5	0.6%	0.2	20.0	0.0012	0.12	0.12
Vines	15	0.8%	0.3	30.0	0.0024	0.24	0.24
	20	0.4%	0.3	30.0	0.00212	0.12	0.12
Orchards	15	2.5%	0.3	30.0	0.0075	0.75	0.75
	20	1.5%	0.3	30.0	0.0045	0.45	0.45

Assuming first order kinetics for the decline of parathion, longer term predicted environmental concentrations (PEC_l) were calculated as the time weighted average concentration for the respective time interval according to the formula.

$$PEC_l = PEC_i \cdot \frac{DT_{50}}{t_l \cdot \ln(2)} \left(1 - e^{(-t_l \cdot \ln(2)/DT_{50})}\right)$$

Where PEC_l = time weighted average concentration, PEC_i = initial concentration, DT_{50} = half-life of disappearance and t_l = considered time period.

Table 2.8.2-2: Time course of the PEC of parathion in water (half life 5.2 days)

Time (days)	**Actual concentration (% of initial)**	**Time weighted average (% of initial)**
0	100.00	100.00
1	87.52	93.62
2	76.60	87.78
4	58.67	77.51
5	51.35	72.99
7	39.33	65.01
14	15.47	45.30
21	6.09	33.55
28	2.39	26.15
42	0.37	17.80
60	0.03	12.50
140	0.00	5.36

Predicted environmental concentrations are in the range of 0.12 - 0.75 µg a.i./l of water. As the half-life of parathion is short, and the compound has a high adsorptive tendency, prolonged exposure of aquatic organisms is not expected.

2.8.3 Fate and behaviour in air

2.8.3.1 Vapour pressure and volatilisation

The vapour pressure of parathion was investigated at 30°C using a soil at 50 and 75% field moisture content. From this study very low values of vapour pressure were determined (3.08-3.92 x 10-6 mm Hg).

The rate of volatilization of parathion depends on its distribution between soil and plans following application . In an experiment, it was observed that after the application no volatilization occurred from the soil whereas up to 40% of the dose applied was lost from the plant surface within 24 hours.

2.8.3.2 Photolysis in air

In a laboratory experiment, parathion had a half-life of 61.4 days in the exposed sample and 1117.2 days in the dark control. Paraoxon, and other unidentified degradation products accounted at a percentage of less than 10% each at the day 30 of the experiment.
A calculation using a computer program of elaborated by the notifier indicated a value of 9.6 hours for the half-life in the troposphere in the use of an average OH-concentration, and a value of 13.9 hours for the chemical lifetime. Direct photolysis was considered to be of lower significance in comparison to the OH-radical induced oxidation in the degradation process.

According to these results an accumulation of parathion in the air and a contamination by wet or dry deposition is not expected.

2.9 Effects on non-target species

2.9.1 Effects on terrestrial vertebrates

In an acute oral toxicity study conducted with Bobwhite quail, an EC formulation of parathion (applied as a single oral dose) was found to be acutely toxic to birds (acute LD_{50} = 2.7 mg/kg b.w.). In a series of short-term feeding studies (5 days exposure) conducted by the U.S. Fish and Wildlife Service with Bobwhite quail, Japanese quail, Ring-necked pheasant and Mallard duck, the LC_{50} values were in the range 76 - 336 mg a.i./kg diet.

For the purposes of the risk assessment, exposure of birds to parathion in the field was assumed to be primarily by uptake in small portions as residues on feed. Accordingly, the single dose exposure of the acute toxicity test was considered inappropriate and the measured LD_{50} value (2.7 mg a.i./kg b.w.) was not used. The feeding studies were considered to be more relevant in terms of the field exposure of birds and mammals and the LC_{50} value obtained with Bobwhite quail, 194 mg a.i./kg food was used. An estimated daily feed intake of young Bobwhite quails in such studies of about 25% of body weight was used resulting in an LD_{50} value (based on daily intake) of 49 mg a.i./kg b.w. It was further assumed that very young mallard ducklings are 2.5 times more sensitive and so the lowest dietary LD_{50} value used in the acute and short-term risk assessment was 19 mg a.i./kg. b.w.

A number of theoretical diets were used for the calculation of avian dietary intakes for the risk assessment. Small birds (about 20 g body weight) were assumed to consume a diet comprising equal quantities of small insects and bigger insects or a diet of either bigger insects or seeds (similar residue levels). Larger birds (> 100 g body weight) were assumed to consume a diet comprising 10% leaves + 45% small insects + 45% bigger insects or a diet consisting entirely of seeds. On this basis, for

small birds the acute toxicity/exposure ratio (TER_a) is in the range 13 (0.36 kg a.i./ha, insects) to 120 (0.2 kg a.i./ha, seeds or bigger insects). For larger birds (body weight greater than 100 g) the acute

toxicity/exposure ratio (TERa) is 36 (0.3 kg a.i./ha, diet of leaves and insects) to 380 (0.2 kg a.i./ha, seeds).

The time weighted average concentration for a time period of 5 days was taken to be 79% of the initial concentration; based on a half-life of 7.11 days. The short-term toxicity/exposure ratio (TER_{st}) was based on dietary intake values, both for toxicity (using the 19 mg a.i./kg b.w. figure) and the estimated intake (daily intake values corrected for the 5-day feeding period using the time-weighted average). On this basis, the TER_{st} values for small birds are in the range 17 (0.3 kg a.i./ha, insects) and 150 (0.2 kg a.i./ha, seeds or bigger insects). For larger birds (body weight greater than 100 g) the TER_{st} values are in the range 46 (0.3 kg a.i./ha, diet of leaves and insects) to 481 (0.2 kg a.i./ha, seeds).

Taking into account the theoretical diet used in the calculation of the TER. TER values indicate some degree of concern with regard to possible risk to birds from the use of parathion, they do not automatically trigger further testing. With regard to the values presented above, a number of factors are used to claim mitigation against any requirement for further evaluation. It is very unlikely that birds under field conditions will consume exclusively contaminated feed and thus the residue levels will in practice be reduced. Due to the short half-life of parathion on/in food items of birds, a longer term exposure and hence any expression of chronic toxicity will not be expected.

Finally, it is pointed out that parathion has been used extensively for many decades world-wide and that because of its potential acute toxicity to birds, parathion has received particular attention. To the registrant's knowledge, no ecologically relevant impact on birds have been reported following at the recommended application rates.

It is concluded that under practical conditions the risk to birds from the use of parathion as an insecticide in grapes, orchards and field crops appears to be low.

When applied as a single dose parathion is acutely toxic to mammals with LD_{50} values in the range of about 2 to about 30 mg/kg body wt. for rats and for the risk assessment a value of 2.4 mg a.i./kg b.w. was considered to be the appropriate worst-case. The corresponding dietary intakes for calculation of the acute TERs (TER_a) were the same as for the birds (generally the same assumptions were made for terrestrial mammals as for birds) . The resultant TER_a values are in the range 1.6 to 15 for for small mammals and 4.5 to 48 for larger animals.

The time weighted average concentration for a time period of 90-days was taken to be 11.4% of the initial concentration; based on a half-life of 7.11 days. The long-term toxicity/exposure ratio (TER_{lt}) was based on dietary intake values, both for toxicity (using the somatic threshold effect concentration

from a 90-day sub-chronic study in rats of 1.25 mg a.i./kg b.w.) and the estimated intake (daily intake values corrected for the 90-day feeding period using the time-weighted average). On this basis, the TER_{lt} values for small mammals are in the range 7.4 (0.3 kg a.i./ha, insects) and 63 (0.2 kg a.i./ha,

seeds or bigger insects). For larger birds (body weight greater than 100 g) the TER_{lt} values are in the range 21 (0.3 kg a.i./ha, diet of leaves and insects) to 208 (0.2 kg a.i./ha, seeds).

The TER values were similar to those for birds, although they were more severe and indicated a higher risk such that in some cases further testing thresholds were triggered. As for birds a number of mitigating factors are considered to reduce this risk. In calculating the TER values, worst case assumptions have been made e.g. with regard to the residue levels in the food items and the feeding activity of the mammals (eating only sprayed material). In practice, the exposure levels will be less than those here and overall, exposure will be relatively short due to dissipation of the residues. However, as with birds, the possible risk is identified in the acute TER values. In the case of the long-term TER values, parathion dissipation is taken into account through the use of the time-weighted average. However, parathion residue intake will be reduced by the feeding behaviour of the mammals as they will feed on a range of items inside and outside the treated area.

Parathion has been used extensively for many decades world-wide and that because of its potential acute toxicity to mammals, parathion has received particular attention. To the registrant's knowledge, no ecological impacts on mammals have been reported following use at the recommended application rates.

It is concluded that under practical conditions the risk to mammals from the use of parathion as an insecticide in grapes, orchards and field crops appears to be low.

2.9.2 Effects on aquatic species

The fish acute toxicity tests conducted with Rainbow trout and Golden orfe and two EC formulations of parathion resulted in 96-hour LC_{50} values of 1.02 - 1.4 mg a.i./l (technical material results: 0.58 - 1.5 mg a.i./l). The 48-hour EC_{50} for an EC formulation to *Daphnia magna* was calculated to be 2.4 µg a.i./l in a flow-through test (technical material result: 2.5 µg a.i./l, in a static test). The effects of EC formulations on the growth of green algae were also assessed, producing 96-hour EC_{50} values based on growth rates of 0.95 - > 1.0 mg a.i./l and based on biomass of 0.47 - 0.49 mg a.i./l (technical material result: 48-hour EC_{50} 0.5 mg a.i./l). The results of the laboratory studies conducted using formulated products of parathion were similar to those obtained with the technical material indicating that the formulation adjuvants did not significantly effect the toxicity of parathion. On this basis, the hazard to aquatic organisms in the field from the use of parathion is estimated using the Toxicity Exposure Ratio (TER) calculated using the toxicity values obtained with the formulated product (these are also more relevant in terms of field exposure).

The Predicted Environmental Exposure (PEC) for parathion following application at the maximum recommended rates of 0.2 and 0.3 kg a.i./ha, have been estimated on the basis of spray drift being the only significant route of contamination of water bodies. Drift values of 0.6% (over 5m) are used for arable crops and up to 2.5% (over 15 m) in orchards and vineyards. The initial maximum PEC values

range from 0.12 to 0.75 µg a.i./l for a 1 m deep water body. The resultant acute TER values for the fish species tested range from 1400 to 8750 and for *Daphnia* the acute TER values are in the range of 3.2 to 20. Taking the worst-case EC_{50} value for effects on algal growth (formulation) of 0.47 mg a.i./l results in acute TER values of between 627 and 3917.

The lowest NOEC obtained from a fish chronic toxicity study was 0.72 µg a.i./l in a fish early life stage study with Sheepshead minnow (using technical material as no studies were conducted with formulated material). The time weighted average PEC for the 28-day exposure period of this test, calculated using a surface water half-life of 5.2 days, is in the range 0.03 - 0.2 µg a.i./l. The resultant long-term TER values are in the range 3.6 - 24. The most lowest NOEC obtained from chronic toxicity studies conducted with *Daphnia* and two EC formulations was 0.01 µg a.i./l. The time weighted average PEC for the 21-day exposure period of this test, calculated using a surface water half-life of 5.2 days, is in the range 0.04 - 0.25 µg a.i./l. The resultant long-term TER values are in the range 0.04 - 0.25.

The results of the studies assessing the acute toxicity of parathion to fish and to green algae indicate a moderate level of acute toxicity. The resultant acute TER values for these organisms are all greater than 100 and so a low risk can be assigned and no further testing is necessary. However, the results of the studies assessing the chronic toxicity of parathion to fish indicate a somewhat higher level of toxicity, particularly in the early lifestage study. This is confirmed by the long-term TER values, which in the most severe case (orchard application) is less than 10. The results of the acute and chronic studies with *Daphnia* indicate significant levels of toxicity. The resultant acute TER and long-term TER values are very low, all being less than 100 and less than 10, respectively.

2.9.3 Effects on bees and other arthropods

Acute toxicity studies in the laboratory revealed that parathion has a very high toxicity to honey bees by the oral, inhalative and contact (direct and indirect) routes of exposure. Taking into account the potential field exposure as given by the maximum application rates, the hazard quotients for all applications indicate a very high risk potential. Parathion does have a short residual toxicity to honey bees. Mortality amongst bees confined for 48 hours with plant residues which had experienced increasing intervals of field weathering was 98% after 8 hours weathering but down to 22% after 24 hours weathering and 1.7% after 48 hours weathering. This indicates that under field conditions the potentially hazardous period to bees from the use of parathion will be short-lived although the LT_{50} does exceed the threshold of 8 hours, above which further testing is required. In the absence of any

additional information to assess the effects of parathion under field conditions it is considered that the product should not be recommended for use during the flowering period of the crop when pollinators may be exposed. Similarly, it should not be applied under other conditions where bees may be exposed e.g. where large quantities of aphid honeydew may be present.

No specific studies have been submitted concerning the possible effects of parathion on non-target terrestrial arthropods. It is assumed that effects will definitely be seen in laboratory and semi-field tests with a wide range of beneficial arthropods as parathion is regularly used as a toxic standard in all kinds of beneficial arthropod testing. In particular, it is stated that effects would be seen in laboratory test with predatory mites, ground dwelling predators, foliage dwelling predators and parasitoids. In addition, it is stated that effects would be seen in field tests with predatory mites.

In the absence of any laboratory, semi-field or field information relevant to an assessment of the risk to non-target arthropods from the recommended use of parathion, it must be assumed that it is of high risk to this category of non-target organisms. Accordingly, any associated restrictions on use that are considered appropriate for this risk classification must be applied.

It is claimed that while parathion is a broad spectrum insecticide, it could be used in integrated pest management programmes as a result of its short persistence and its limited impact on arthropod natural enemies. It is considered that the quick and reliable action of parathion opens the possibility for its use only when the level of pest infestation threatens to reach the economic threshold level. Further, while it can adversely affect predators and parasites, it is suggested that it would never exterminate a whole population and that re-population would occur quickly due to its short persistence.

2.9.4 Effects on earthworms and other soil macro-organisms

The LC_{50} of two EC formulations of parathion for the earthworm, *Eisenia foetida*, was found to be > 105 and 253 mg/kg dry wt. soil, indicating a low level of toxicity. At application rates of 200 and 300 g a.i./ha, the PEC in the top 5 cm soil layer, assuming 50% of the applied material reaching the soil (after foliage interception) and a soil bulk density of 1.5 g/cm^2 , is 0.13 and 0.2 mg/kg, respectively. This gives TER values in the range of at least 525 to 1946. This indicates a high margin of safety between the toxicity of parathion to earthworms and the expected exposure levels in the field following its use.

No values are given for the soil concentration over time and so a long term TER (based on a long term soil PEC), cannot be calculated. However, given the relatively short half-life for parathion in soil, half-life of up to 32 days in field dissipation studies, it is reasonable to assume that there will be no longer-term effects on earthworms. Even if a TER_{lt} were calculated using the maximum initial PEC_s

and the worst-case NOEC obtained with the EC formulations (1 mg a.i./kg) this would result in a value of 5 which would not trigger further testing.

The maximum reported DT_{90} value was 138 days which would not require organic matter breakdown to be investigated. Given the generally short persistence of parathion in soils, the lack of effects seen in the micro-organism studies and the low risk to earthworms, it is generally considered that additional testing on soil non-target macro-organisms other than earthworms is not necessary.

2.9.5 Effects on soil micro-organisms

Laboratory studies (28-56 days) were conducted with two EC formulations of parathion assessing the effects on soil micro-organisms through assessments of organic matter turnover (nitrification and soil respiration processes) for up to 56 days incubation. These revealed that at the application rates of up to 20 kg a.i./ha, parathion had no negative influence on microbial mineralisation processes in a number of field soils (loamy sand, sandy silt loam, silty sand and loamy silt soils). It can, therefore, be concluded that under recommended conditions of use parathion will not adversely affect soil microbial activity and no further testing is necessary.

2.9.6 Effects on other non-target organisms (flora and fauna)

The spectrum of the biological activity of parathion is represented by the information given in the relevant sections and confirmed in practical use over several decades. Therefore, further data concerning possible effects on other non-target organisms (flora and fauna) are not presented as it is considered that they would not change the ecotoxicological assessment.

2.9.7 Effects on biological methods of sewage treatment

Due to the very short half-life of parathion (5.2 days) there is no perceived impact on water treatment procedures.

2.10 Classification and labelling

Parathion

Hazard symbols	Tx	
Indication of danger	Very toxic	
Risk phrases	R27/28	Very toxic in contact with skin and if swallowed
	R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety phrases	S28	After contact with skin, wash immediately with plenty of soap and water.
	S36/37	Wear suitable protective clothing and gloves.
	S45	In case of accident or if you feel unwell seek medical advice immediately.
	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.

EC Formulations of Parathion

Hazard symbols	T+	
Indication of danger	Very toxic	
Risk phrases	R24	Toxic in contact with skin.
	R26	Very toxic by inhalation.
	R28	Very toxic if swallowed.
	R36	Irritating to eyes.
	R38	Irritating to skin.
Safety phrases	S28	After contact with skin, wash immediately with plenty of soap and water.
	S36/37	Wear suitable protective clothing and gloves.
	S45	In case of accident or if you feel unwell seek medical advice immediately.

LEVEL 3

Parathion

Proposed decision with respect to the application for inclusion of the active substance in Annex I

3.1 Background to the proposed decision

Parathion is the ISO common name for O,O-Diethyl O-(4-nitorphenyl)phosphorothioate (IUPAC) or Phophorothioic acid, O,O-diethyl O-(4-nitrophenyl) ester (CA). Parathion is an organophosphorus insecticide with acaricidal and ovicidal effects. Formulated as an emulsifiable concentrate it is used on a range of crops throughout the EC.

3.2 Proposed decision concerning inclusion in Annex I

3.3 Rational for the postponement of the decision to include the active substance in Annex I, or for the conditions and restrictions to be associated with a proposed inclusion in Annex I, as appropriate

An ADI of 0.006 mg/kg/day can be established. An AOEL of 0.006 mg/kg/day can be set.

Both ADI and AOAEL have to be considered temporary since there are no information on developmental neurotoxicity, including brain acetylcholinesterase inhibition, in laboratory animals following peri-postnatal exposure.

Due to the lack of data for the intended uses, no residue definition for risk assessment can be recommended, no potential dietary exposure can be estimated.

The information supplied with regards to fate and behaviour in the environment indicate that ethylparathion should not be included in Annex I because PEC in water is very close or greater than concentration found to be toxic to Crustacea.

The impact on non-target aquatic organisms should be assessed; the application to areas adjacent to water bodies should be avoided.

The decision on the inclusion of ethylparathion in Annex I of Council Directive 91/414/EEC is postponed, pending receipt and evaluation of further data listed in Level 4

LEVEL 4

Parathion

Further information to permit a decision to be made, or to support a review of the conditions and restrictions associated with the proposed inclusion in the Annex I

4.1 Identity of the active substance

4.2 Physical and chemical properties of the active substance

4.3 Data on application and further information

4.4 Methods of analysis

Method for food of plant origin and its independent laboratory validation.

4.5 Toxicology and metabolism

The Applicant should provide information on the risk for developmental neurotoxicity, including brain acetylcholinesterase inhibition, following peri-postnatal exposure to parathion.

No data on medical surveillance on manufacturing plant personnel are reported in the dossier. The lack of these data is not acceptable, since this product has been used for many years,. A report on the results of medical surveillance of manufacturing workers should be provided, including results of biological monitoring..

Comprehensive information is missing concerning accidental or occupational cases of acute poisonings, and epidemiological results on the occupational or general population. The lack of these data is not acceptable for a product which has been used for many years. Further information on these issues should be provided.

Estimation of operator exposure:

The results of risk evaluation based on Generic Databases to predict operator exposure indicate the need to proceed to a Tier-III risk assessment, based on actual measurements of exposure, rather than on exposure estimates.

A field exposure study is necessary to measure dermal and inhalation exposure, as well as the absorbed dose through biological monitoring. The field study should be provided within 1999. Exposure should be assessed both during applications in high crops and during applications in greenhouses, since this use pattern is envisaged to treat ornamental plants and protected crops.

Estimation of bystander exposure:

The Company claims that problems for bystanders are not anticipated due to the low vapour pressure; this claim cannot be accepted in light of the reported intended uses, application patterns, and the potencial inhalation toxicity. Bystanders exposure should be estimated.

Estimation of worker exposure:

Worker exposure has not been estimated by the Company. The provided justification is that Parathion 500 EC is normally used at times when entering the crop shortly after spraying is not necessary. In light of the intended use and application patterns, worker exposure should be estimated.

4.6 Residue data

Additional metabolism data on crops supported as intended uses

4.7 Environmental fate and behaviour

4.8 Ecotoxicology

Effects on non-target species

Since the risk to aquatic life is of concern, Member States should require the notifier to submit data from the real environment or mesocosm studies demonstrating acceptability to aquatic life from the combination of leaching and spray drift contamination even in the case of worst conditions (maximum application rate an minimum dilution of the receiving water body).

4.9 Classification, packaging and labelling