OECD Guidance for Industry Data Submissions for Microbial Pest Control Products and their Microbial Pest Control Agents

(Dossier Guidance for Microbials)

Guidelines and Criteria for Industry for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for Microbial Pest Control Products and their Microbial Pest Control Agents in Support of Regulatory Decisions in OECD Countries

August 2006

- OECD Environment Directorate -

FOREWORD

This document is intended to provide guidance to applicants wishing to have particular microbial pest control agents approved or microbial pest control products registered. It provides guidance with respect to the format and presentation of the documentation to be submitted. For plant protection products containing other active substances, applicants are referred to the OECD Guidance for Industry Data Submissions on Plant Protection Products and their Active Substances (Dossier Guidance).

The document provides guidance with respect to the format and presentation of the documentation to be submitted. MRLs and or import tolerances are not normally established for these types of products. However, if necessary, relevant guidance can be found in the OECD Guidance for Industry Data Submissions on Plant Protection Products and their Active Substances (Dossier Guidance).

Regulatory authorities generally require sufficient information on a microbial pesticide to characterize it, to assess its potential risks to people and to the environment, and to confirm its effectiveness for pest control. Unlike chemical pesticides, microbial pest control agents may infect or cause disease in other living organisms. Potential adverse effects of microbial pesticides include displacement of non-target microorganisms and allergenic, toxic, and pathogenic effects on humans and other non-target organisms. However, microbial pest control agents typically have narrow host ranges and occur naturally in the environment to which they are applied. Such factors reduce the likelihood of harm should a microorganism be used for pest control. Consequently, the risk assessment of microbial pest control products rests heavily on the biological and ecological profile of the microorganism and a set of short term toxicity/pathogenicity tests, with the expectation that negative test results will allow a high degree of confidence in the safety of the microorganism.

The numbering system in this document is based on the "*Guidelines and Criteria for Industry for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for Plant Protection Products and their Active Substances in Support of Regulatory Decisions in OECD Countries*" (Please consult the OECD Pesticide Web site at **http://www.oecd.org/env/pesticides** or contact the OECD Secretariat for the latest version of this document). ~~The numbering system in *this* document is not identical. However, in an attempt to avoid confusion, and to illustrate parallel data requirements for plant protection products, the numbering system used for plant protection products is retained, where possible.~~

The summaries of data and information included in the appendices to these guidelines are intended to be illustrative of the approach to be taken in the preparation of the comprehensive summaries required. The appendices concerned have not been critically examined for their technical content.

This guidance was developed with the aim of facilitating the compilation of data submissions to OECD countries by providing a common format and structure for their preparation, thereby reducing the need for resource-intensive re-formatting, re-structuring and re-writing for individual countries. A common format also facilitates (1) the use of electronic data submissions, and (2) the preparation of countries' review reports to a similar format and structure (monographs), thus allowing better mutual use of review reports and burden-sharing among countries. The preparation of dossiers and monographs according to a common format and structure will contribute to cost savings for both governments and industry.

Where on particular points of detail, additional or more detailed guidance is required, applicants and other interested parties are advised to contact the relevant authority of the country to which the documentation is to be submitted.

This guidance document is based on and is consistent with the Guidelines and criteria for the preparation and presentation of complete dossiers and of summary dossiers for the inclusion of microbial pest control agents in Annex I of Directive issued by the European Commission (Commission Document 1663/VI/94, rev 8 of 22 April 1998) and was prepared with the benefit of the comments provided by the delegations of countries participating in the OECD Working Group on Pesticides and by pesticide industry representatives. The summaries of data and information included in the appendices to these guidelines relate to a different microbial pest control agent to that addressed in the European Commission Guidelines. The appendices to this guidance document are consistent in overall form and structure with those appended

to the European Commission Guidelines, but the individual study summaries include more headings and sub-headings and include an executive summary.

For EU Member States, please refer to Dir 90/219 and Dir 90/220 for submissions to EU countries that contain genetically engineered organisms.

*Note: This document will be periodically revised, as some sections will be added or updated. Please consult the OECD Pesticide Web site at **http://www.oecd.org/env/pesticides** or contact the OECD Secretariat to make sure that you have the latest version. It is not intended that summaries of data and information in preparation or already prepared be revised to achieve compliance with revised versions of this document.*

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1 GENERAL INTRODUCTION

1.1 The guidance provided and criteria specified, apply to the preparation of complete dossiers and summary dossiers, whether submitted in support of applications for approval of a microbial pest control agents (MPCA), for the registration of a microbial pest control product (MPCP). For the purposes of this guidance document, a complete dossier consists of all the test and study reports (including individual animal data, where appropriate) to be submitted, together with the summaries of the tests and studies submitted and relevant supporting documentation, while a summary dossier consists of that same set of documentation, without the test and study reports.

1.2 This guidance document is intended to be relevant for major data submissions. The tiered structure proposed for the compilation of summary dossiers is unlikely to be relevant in the case of more limited data submissions. The format suggested for summarizing the various types of data and information is always likely to be relevant. It is not intended that summaries of data and information in preparation or already prepared be revised to achieve compliance with revised versions of this document that are issued from time to time.

1.3 While requiring standardization in general lay out, subject matter, terminology and units of measurement, applicants nevertheless are required to use expert judgement in preparing the documentation concerned. Within the constraints imposed by the provisions of the legal requirements of individual countries, applicants nevertheless should treat these guidelines as providing a degree of flexibility.

1.4 These guidelines and criteria apply to documentation submitted for consideration, whether submitted by applicants, or by other interested parties wishing to submit technical or scientific information, with regard to the potentially dangerous effects of MPCAs and/or their metabolites (especially toxins), MPCPs, on human or animal health or the environment. Hence, these guidelines and especially examples for summaries are specifically designed to be appropriate for micro-organisms/viruses. Therefore, for studies on metabolites (especially toxins, which are chemical substances), it may often be more appropriate to prepare documentation like Tier I - III summaries according to the OECD guidance on dossier preparation for chemical substances (*Guidelines and Criteria for Industry for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for Plant Protection Products and their Active Substances in Support of Regulatory Decisions in OECD Countries - Revision 1, March 2001*)."

1.5 The objective is to achieve standardization, to the extent that is practicable and feasible, of the format and presentation of documentation submitted, with a view to:

- ensuring the quality and consistency of the documentation submitted;
- facilitating efficiency and economy in the use of resources necessary for the preparation of that documentation;
- facilitating applicants in checking the completeness and quality of the documentation prior to its submission;
- facilitating the use of electronic media for the submission, archiving and retrieval of the documentation submitted;

- facilitating efficiency and economy in the use of resources necessary for its evaluation; and

- facilitating the development of burden sharing arrangements by regulatory authorities, thereby further increasing efficiency and economy in the use of evaluative resources.

1.6 Notwithstanding the clear need for evaluators, whether toxicologists, chemists or biologists, to assess original study reports and supporting data and information, summaries of the data base submitted are also required (dossier summaries), to facilitate:

- checking for completeness by applicants and by the regulatory authority concerned;

- evaluation and assessment of the documentation concerned by the regulatory authority concerned;

- evaluation and assessment of the documentation concerned by the committees established or convened for that purpose; and

- decision making by the relevant authority.

1.7 Accordingly, those wishing to submit data and information in support of proposals for the approval of a MPCA, for the registration or re-registration of a MPCP, are themselves required to summarize, evaluate and assess the data concerned in the light of the relevant evaluative and decision making criteria. They are also required to make proposals for the decision to be made in the light of their assessment of the data and information concerned, proposals which should be supported with statements as to the rationale used.

1.8 The tiered approach specified for the preparation of dossier summaries in these guidelines is designed to facilitate efficiency in the use of evaluative resources and to facilitate decision making.

1.9 Forms, developed to facilitate checks to be carried out to ensure that all the necessary information, data and summaries have been included in dossiers submitted and which are to be completed and submitted by applicants, are also intended to be of benefit to applicants for the purposes of checking that all the necessary information, data and summaries have been included in dossiers being prepared for submission. Such forms in some cases have been developed, and in other cases are to be developed, by the regulatory authorities of the various OECD countries.

1.10 Standard Units, Terms and Abbreviations:

- Standard Units - the English language version of Standard International Units must be used in reporting and summarizing tests and studies, although other units, if desired or considered relevant, may be used in parentheses [1],
- Standard Terms and - in the interest of avoiding confusion, standard technical terms
- Standard Abbreviations - and abbreviations as specified in Appendix 1, must be

[1] Particular attention is drawn to the requirement to use metric units - e.g. in the case of application rates, kg microbial pest control agent /ha; content of microbial pest control agent in formulations, g/kg or g/l; content of residues, mg/kg; doses in feeding studies, mg/kg body weight. Where it is necessary that other units be used, conversion factors should be provided.

used - these Appendices will be further developed as required. Where terms and abbreviations not listed are used, a concise explanation of each such term or abbreviation should be provided in the text when it is used for the first time. In addition, a listing of all such additional terms and abbreviations should be provided as an Annex to each relevant summary document.

1.11 Hard copies of complete and summary dossiers should be submitted. In addition, applicants could provide information in a suitable electronic form in accordance with the requirements of the relevant regulatory authority - applicants are advised to discuss the approach they propose using with the regulatory authority of the country to which they propose making application. A number of options for the electronic submission of information are available, and two possibilities are described below. However these do not preclude the use of other options:

Option 1 the summary dossier, which contains the summary and assessment Information and supporting documentation, but not the test and study reports, could be provided in a suitable word processor, and where appropriate, spreadsheet format, on diskette(s) or by other electronic media;

Option 2 the entire dossier, including test and study reports, individual animal data, historical control data, other relevant data and information, as well as the summary and assessment information and supporting documentation, could be provided using the CADDY electronic dossier interchange and archiving format, which utilizes CD-ROM technology. The CADDY system, prepared in accordance with an EU Specification, allows submission of study reports as image files and has provision for the summary dossier to be included on the CD-ROM in the form of word processor/spreadsheet files, as appropriate. The content of dossiers submitted in CADDY format is identical to that of hard copy versions submitted. Further information on CADDY can be obtained from the Crop Life International (CLI):

Crop Life International
Avenue Louise 143, B-1050 Brussels, Belgium
Phone: 32 2 542 04 10
Fax: 32 2 542 04 19
WWW: http://www.croplife.org/

Regardless of the option chosen, applicants are encouraged, where possible, to present information in tabular form. Separate items of information such as the names of authors should be allocated to separate cell columns. A row should be allocated to each entry. Alternatively a spreadsheet format can be used. The recommended approach is intended to facilitate the subsequent manipulation of the information provided by the regulatory authority to which application is made.

1.12 Applicants wishing to obtain information as to the requirements of the various regulatory authorities with respect to the number of complete and summary dossiers to be submitted should contact the regulatory authority in the country to which application is to be made.

2 DOCUMENTATION REQUIRED

2.1 Introduction

2.1.1 The summary documentation to be prepared and submitted, should allow a comprehensive understanding of the application and facilitate evaluation and decision making having regard to the evaluative and decision making criteria which are relevant in the country to

which application is made, notwithstanding the clear need for reference to the individual study reports and the detailed data (e.g. data on relevant variables for individual animals), during the course of evaluating the data base concerned.

2.1.2 Whether the application involves a proposal for the approval of an microbial pest control agent, for the registration or re-registration of a pest control product, or a proposal to vary the conditions of any such registration, or relates to the review of any such registration, the applicant's objective should be to produce summaries and assessments which, accurately reflect the conclusions that can be derived from the data and information submitted and includes a proposal, prepared by the applicant, for the decision to be taken by the relevant regulatory authority in the country to which application is made.

2.2 Individual Documents Required

The documentation required comprises a number of separate elements and should include, in the following order:

Document A Purpose

A statement of the context in which the dossier is submitted -

- approval of a new MPCA,
- approval of an existing MPCA,
- registration of a MPCP containing a new MPCA,
- registration of a MPCP containing an existing MPCA,
- modification or removal of conditions or restrictions associated with the registration of a MPCP,
- special review of the registration of a MPCP, where indications exist suggesting that the conditions of registration are no longer satisfied,
- routine review of the registration of a MPCP, anticipating expiry of the period for which registered,

Document B Task Force Information

Where relevant, details of any task force that exists or is formed for the purposes of defending particular microbial pest control agents. The information provided should include the following information -

- the membership of the task force and a contact point for the task force (name, address, telephone and telefax numbers and e-mail address),

- a contact point for each member of the task force (name, address, telephone and telefax numbers and e-mail address),

- the list of test and study reports which were generated by or on behalf of the task force - where some members of the task force share ownership of, or have access to, some but not all of the test and study reports, a clear indication should be provided as to the ownership of, and rights of access to, the individual test and study reports listed;

Document C Labels and Leaflets

Where requested, copies of existing or proposed label(s) and where relevant leaflets for each of the preparations for which a dossier is submitted and in addition, labels and leaflets relevant to the uses on the basis of which import tolerances are supported or proposed. Where relevant, a translation of the texts of labels and leaflets submitted;

Document D-1 Supported Uses

Details of the intended uses (uses that are being supported by the applicant, for which data have been provided or, where relevant, for which data are to be provided by a specified date) and conditions of use (GAPs), on both food and feed crops and on non food and feed crops in the territory of the country to which application is made, supported in relation to the proposed approval - the information concerned should be provided using forms as set out in Part 1 of Appendix 3. Uses which are not yet registered should be identified by means of an asterisk or footnote;

Document D-2 Registered Uses

For existing MPCAs, a list of current registered uses in the country to which application is made and an indication of whether, or not, actually used (Document D-2) - the information concerned should be provided using forms as set out in Part 2 of Appendix 3. The listing provided should include those uses which are currently registered but which are not being supported by the applicant. The information provided with respect to actual use, should identify those registrations that are not currently availed of (some uses or all uses), and further should describe those instances where the rate and manner of use in practice is more restrictive than is provided for in the existing registration (e.g. registered uses of a pest control product for which the product is not currently commercialized; uses for which the maximum registered application rate is seldom if ever availed of);

Document F Statements of Intention to Submit a Dossier

Where in the case of the review of existing registrations or MRLs, the commercial interests and other parties involved or concerned, are required to submit a statement of intention to submit, in due course, a dossier or dossiers, a copy of all such statements;

Documents G – I Documentation on Formulants

Unless a full data package is submitted for every formulant included in the preparation (ingredient other than MPCA) the following -

Document GA statement as to whether the substance is permitted in food, animal feeding stuffs, medicines or cosmetics in accordance with the legislation of the country to which application is made,

Document HA copy of the safety data sheet, and
Document I Where requested, other available toxicological, exposure and environmental data;

Document J Confidential Information

Where relevant and desired, a statement to indicate the data and information involving industrial and commercial secrets for which confidentiality is requested, in accordance with the legislative provisions of the country to which application is made. To facilitate the secure handling of such information, it should be included in a separate file, where it is feasible to do so (e.g. details of manufacturing processes, detailed specifications of MPCA and preparations and individual medical records). The file should be identified as containing industrial and commercial secrets. Where applicants wish to have data and information involving industrial and commercial secrets treated as confidential, applicants should -

- taking account of the legislative provisions of the country to which application is made, provide a listing of the data and information for which confidentiality is requested, clearly cross-referenced, for each item, to the relevant test and study reports, as well as to the dossier summaries and supporting documentation submitted - the listing should be included in the file referred to above,

- for each item listed, provide a justification for the claim that it is, or constitutes, an industrial and commercial secret - the justifications should be included in the file referred to above, and

- highlight other items of information for which confidentiality is requested, in relevant study reports, dossier summaries and supporting documentation (e.g. identity of test laboratories);

Document KTest and Study Reports (MPCA)
Document K Test and Study Reports (MPCP)

Individual test and study reports in accordance with the legislative requirements of the country to which application is made (Figure 1) - for the convenience of evaluators, separate dossiers should be provided for the MPCA and MPCPs. Where the registration of more than one microbial pest control product is requested, a separate dossier on each microbial pest control product for which a registration is requested should be provided;

Documents L – N Dossier Summaries

A summary, evaluation and assessment of the dossier of data and information submitted by the applicant, prepared in accordance with the tiered structure described here under, and presented graphically in Figure 1, to include -

Document L (MPCA) (Tier I)
Document L (reference lists)
Document L (MPCP)

For the individual tests and studies submitted, reports as to their quality, prepared by or on behalf of the applicant, together with a list of the test, study reports and documents submitted - see also paragraphs 3.1.1 and 3.2.1,

Document M (MPCA) (Tier II)
Document M (MPCP) (Tier II)

A comprehensive summary and assessment of the individual tests and studies and groups of tests and studies, as appropriate, in the light of relevant evaluative and decision making criteria - see also paragraphs 3.1.2 and 3.2.2,

Where relevant, to include an evaluation, cross referenced to the supporting documentary evidence, of the relevance of particular studies conducted regionally (e.g. residue data), to the agricultural, plant health and environmental (including climatic) conditions of other regions, together with the rationale for extrapolations proposed,

Document N(Tier III)

- an overall summary and assessment of the application in the light of relevant evaluative and decision making criteria, the conclusions reached by the applicant on the basis of the data and information submitted, together with a statement of the proposed conditions and restrictions to be associated with any approval or registration granted, supported with the rationale for the proposals made - see also paragraphs 3.3.1 to 3.3.5, and

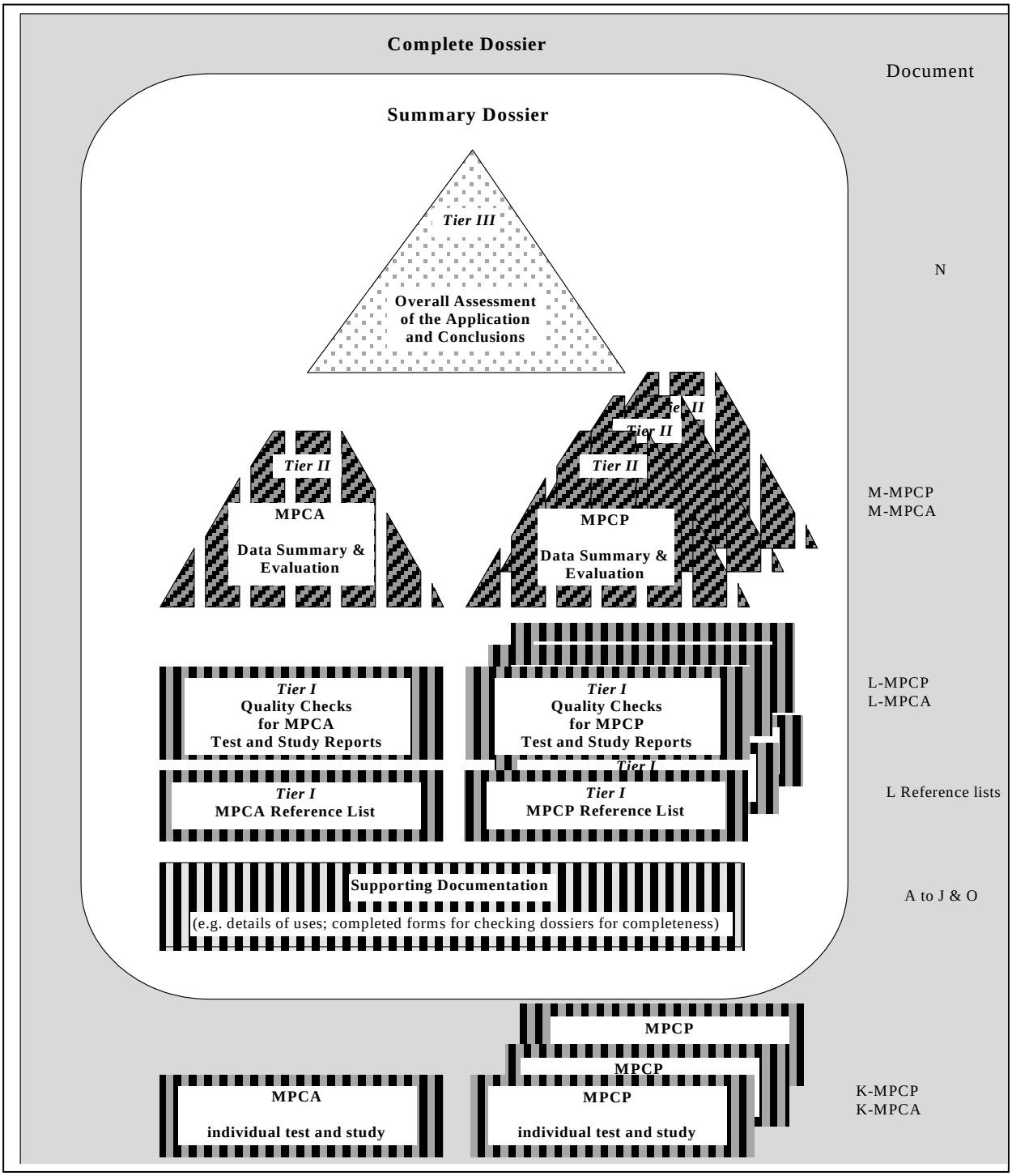
Document O Completeness Check Forms

A completed set of the forms for the checking of dossiers for completeness (evaluation forms 1, 2, 3, and 4 - see paragraphs 4.1 to 4.2.4).

2.2 Documentation Required - Individual Documents Required

Figure 1

DOSSIER STRUCTURE AND CONTENT



Where requested, a sample of each MPCA as manufactured and which complies with the specification(s) submitted, should be submitted in a recognized culture collection.

2.3 Documentation Required - Samples and Analytical Standards

3 DOSSIER SUMMARIES AND OVERALL ASSESSMENTS - DETAILED REQUIREMENTS

3.1 Dossier on the MPCA

3.1.1 Tier I - Document L (MPCA) - Checks as to the acceptability of the quality of individual test and study reports relating to the MPCA

A. The dossier summary should, in principle, include a report as to the acceptability of the quality of each individual test and study submitted to address each relevant data requirement. Those reports should be assembled in sections as specified in subparagraph (xvi).

B. The Tier I checks as to the acceptability of the quality of individual test and study reports to be submitted are intended to facilitate efficiency in the use of the resources available to the regulatory authorities for the evaluation of dossiers (scientific secretariats and specialist evaluators). In particular they are intended to facilitate the checking of dossiers as to completeness and format, checks to ensure compliance with the principles of GLP or GEP [2], as appropriate and, checks relating to the suitability of test methods used.

C. In the case of testing as to the physical and biological properties of MPCAs, and by way of exception, it is not necessary that reports as to the quality of individual tests be provided. Details of the methodologies used should be provided in the Tier II summary (see paragraph 3.1.2) and instances of non compliance with or, of divergence or omissions from the requirements relating to the principles of GLP or GEP, as appropriate, should be indicated and be justified for each individual test or study.

D. Where the test methods used were those currently specified, and where the tests or studies concerned were conducted in accordance with the principles of GLP/GEP, as appropriate, Tier I checks as to the acceptability of the quality of individual test and study reports should take the following form (examples are provided in Part 1 of Appendix 4):

1.1 the data point addressed (cf subparagraph xvi),
1.2 a description of the type of test or study;
2 reference point (location) of the report in the dossier (e.g. section 3, point 5.2.1 /01);
3.1 the names of the authors,
3.2 the title of the test or study report,
3.3 the owner of the report,
3.4 an indication as to whether it is a published or unpublished report,
3.5 the report number,
3.6 the date of the report;
4.1 the name and address of the testing facility,
4.2 the laboratory report/project number;
5 the dates of commencement and completion of experimental work;
6.1 the identity of the test substance or material (microbial taxonomic classification and isolate identification, designation, and deposition number in a recognized culture collection),
6.2 an explicit reference to the relevant specification of composition of the test substance or material;
7.1 the identity of the test guideline used,

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2 The principles of GEP (Good Experimental Practice) are analogous to the principles of GLP, but are less onerous in terms of the requirements and procedures relating to quality assurance, inspection and auditing. In the European Union, GEP is obligatory for those tests and studies to which GLP does not apply (e.g. technical properties of MPCPs, efficacy and phytotoxicity tests)

7.2 where test guidelines provide choice as to the method to be used, a reasoned justification for the method used,

7.3 where deviations from the test guidelines specified are employed, a description of and reasoned justification for the deviations;

8 confirmation that the principles of GLP or GEP, as appropriate, were complied with - in the event of non-compliance a description of the degree of non-compliance and a justification for non-compliance.

i. For tests and studies for which the test methods used were not those currently specified (i.e. studies conducted in accordance with test guidelines which have been replaced or were never accepted), a more detailed approach is necessary in which each of the following points should be addressed in the Tier 1 checks as to the acceptability of the quality of individual test and study reports - where a particular heading is not relevant, the reason that it is not relevant should be stated. Please see Appendix 11, Form 5.

(vi) A number of specimens of Tier I checks as to the acceptability of the quality of individual test and study reports for studies conducted in accordance with test guidelines other than those specified, are contained in Part 2 of Appendix 4.

(vii) It is not necessary that Tier I checks as to acceptability of the quality of reports be provided for reports relating to analytical methods, identity and biological properties, regardless of whether the methods concerned relate to analysis of MPCA as manufactured or analysis of MPCPs. Details of the methods of analysis concerned should be provided in the Tier II summary and evaluation (see paragraph 3.1.2 viii and Appendix 7, Part 2).

ii. The final part of Tier I of the summary dossier should comprise a listing of all test and study reports, test guidelines, and published papers, submitted as part of the dossier and a separate listing of all test and study reports, test guidelines, and published papers, not submitted as part of the dossier, of which the applicant is aware and which are relevant to the regulatory decision proposed (i.e. those that address relevant end-points). It is to be noted that applicants are obliged to submit all relevant information of which they are aware concerning potentially dangerous effects, not just a reference to such reports and papers.

a. In preparing the listing, applicants should conduct a detailed literature search - expert judgement is required to determine the nature and extent of the search to be conducted. The date on which the reference list was compiled, the identity of the data bases searched, the date range established for the purposes of the search (e.g. abstracts dated earlier than 1980 not requested), the language constraints, if any, imposed and the key words used for the purposes of the literature search, should be indicated.

i. The listing of test and study reports, test guidelines, and published papers submitted as part of the complete dossier, should cover each section of the dossier separately. References which relate to more than one section should be listed in each relevant section. Within sections, for each point, and where appropriate, sub-point, the list should be arranged alphabetically by author. Where for a particular author there is more than one report or paper, they should be listed in chronological order, with the most recent report or paper listed last. In cases where for a particular author, more than one reference is listed for any one year, the references should be distinguished by inserting letters after the year i.e. a, b, c, etc., as appropriate. For each test and study report, an indication should be provided as to whether or not it is published and as to whether or not it was conducted in compliance with the principles of GLP or the principles of GEP, as appropriate. The listing of individual test and study reports should be annotated to indicate their owner and to indicate whether or not data protection is claimed in accordance with the relevant rules in place in the country to which the dossier is submitted. Before regulatory decisions are made, applicants will be required, where appropriate, to certify that the studies for which they have claimed data protection, have or have not been submitted in support of other

applications. A suggested format for the presentation of the listings of test and study reports, test guidelines, and published papers submitted is contained in Part 1 of Appendix 6. In order to facilitate the subsequent manipulation of the reference list by the regulatory authority, the listing should be compiled using a word processing table function, using a separate row for each reference.

ii. A second version of the listing of test and study reports, test guidelines, and published papers, submitted as part of the complete dossier, which should again cover each section of the dossier separately, but in which the tests and studies are listed alphabetically by author and for individual authors, in chronological order, should be provided. A suggested format for the presentation of the second listing of test and study reports, test guidelines, and published papers submitted is contained in Part 2 of Appendix 6. In order to facilitate the subsequent manipulation of the reference list by the regulatory authority to which it is submitted, the listing should be compiled using a word processing table function, using a separate row for each reference.

iii. In the case of test and study reports and published papers not submitted, a separate listing of such documents, arranged alphabetically by author, should be provided at the end of each section. A suggested format for the presentation of the listings of test and study reports and published papers not submitted is contained in Part 3 of Appendix 6. In order to facilitate the subsequent manipulation of the reference list by the regulatory authority to which it is submitted, the listing should be compiled using a word processing table function, using a separate row for each reference.

iv. The separate sections for which a listing of test and study reports, test guidelines, and published papers is required are as follows:

Section 1

1. Identity of the MPCA and its metabolites (especially toxins)

2. Biological properties of the MPCA and its metabolites (especially toxins)

3. Further information on the MPCA (function; effects on harmful organisms; field of use; harmful organisms controlled and crops or products protected or treated; mode of action; information with respect to resistance and resistance management strategies; recommended methods and precautions concerning handling, storage, transport or fire; procedures for destruction or decontamination),

4. Proposals including justification for the proposals for the classification and labelling of the MPCA

5. manufacturers methods for the MPCA; quality control information for the MPCA

Section 2 Analytical methods;

Section 3 Health studies on the MPCA;

Section 4 Residues (normally not required)

Section 5 Fate and behaviour in the environment; and

Section 6 Ecotoxicological studies on the MPCA

i. For the purposes of avoiding confusion and facilitating the examination of dossiers submitted, a compilation of all scientific name of microorganism to species and/or strain level or a level sufficient to show taxonomic relation to known microorganisms, especially pathogens; accession no. of sample in a recognized culture collection; test

procedures and criteria, using best available technology, to characterize the strain or serotype; for mutant or genetically-modified strains (For EU Member States, please refer to Dir 90/219 and Dir 90/220 for submissions to EU countries that contain genetically engineered organisms) indicate all known differences between the modified microorganism and the parent wild strain(s)-include any trade names, common names, and developmental code names. The approach suggested for the preparation of compilations of names, common names, synonyms and code names for the MPCAs is illustrated in the listing comprising Part 4 of Appendix 1.

ii.

iii. The numbering systems used in many OECD countries for the data and information relating to MPCAs to be submitted, are different. Applicants should use the OECD numbering system, which may be found in Part 4 of Appendix 6, in submitting data and information appropriate to the country (or countries) to which application(s) is (are) being made. Alternatively, applicants can use the country-specific numbering system for the country to which application is being made. A compilation of the numbering systems used in some OECD countries is provided in Part 4 of Appendix 6.

(xviii) The OECD numbering system for the data and information to be submitted provides in a number of cases for flexibility as to whether particular studies are submitted as part of the dossier on the MPCA or as part of the dossier on the MPCP. That flexibility, within the constraints imposed by the regulatory requirements of the country or countries to which submission is to made, is intended to accommodate applicant preferences. Regardless of the choices made by applicants, it is necessary that suitable cross references be provided, as appropriate.

3.1.2 Tier II - Document M (MPCA) - Summary and assessment of the dossier relating to the MPCA

i. The Tier II summary for an MPCA should contain sections such that it contains a discussion and interpretation of the results of all the tests and studies which relate to the microbial pest control agent and within each section, the conclusions reached. The sections are those specified in paragraph 3.1.1 (xvi).

(ii) Where relevant and necessary (e.g. registration of a MPCP, efficacy data and information is required in some countries. However, such information is relevant to the MPCP rather than to the MPCA. It therefore is neither necessary nor appropriate that the Tier II summary for the MPCA include such information.

(iii) The Tier II summary should be confined to and rely only on that data and information contained in the MPCA dossier provided. If desired, a reference to the corresponding formulation summary or summaries can be included.

(iv) In the case of non submission of particular studies, full justifications should be provided (see Appendix 2 and Appendix 11, Part 3

(v) Where the principles of GLP or of GEP have not been followed, or where the methodologies used were not those currently prescribed in the country to which application is being made or, where there were deviations from the methods prescribed or other methods used, a justification of the overall quality and scientific validity of the test or study reported should be provided.

(vi) As a general rule, a concise but comprehensive summary of each individual test and study should be included. Each summary should include the following elements, as appropriate:

- the reference number of the test or study;
- the appropriate test or study reference (e.g. Casida et al 1979);
- the test guideline and method used;

- relevant GLP/GEP information;
- a brief description of the methodology used;
- a concise tabular presentation of the findings with supporting text, in which the significance of results obtained, effects and observations reported, are highlighted; and
- conclusions reached (to be highlighted);

(vii) By way of exception to the general rule, in the case of certain parts of the dossier such as that relating to the identification and biological properties of the MPCA, a tabular approach to the presentation of the data may be appropriate.

(viii) Examples of parts of a Tier II summary for a MPCA are provided in Appendix 7.

- Part 1 contains the suggested format for that part of a Tier II summary which relates to the identification and biological properties of the MPCA.
- Part 2 contains the suggested format for part of a Tier II summary relating to analytical methods.
- Part 3 contains an example of part of a Tier II summary relating to health studies.
- Part 4 contains an example of a data waiver relating to residues.
- An example of part of a Tier II summary relating to fate and behaviour in the environment is provided in Part 5 of Appendix 7.
- Part 6 contains examples of ecological studies and risk assessment.

(ix) For each of the sections of the Tier II summary, it is particularly important that the concluding element for each point and the concluding element of sub-sections and sections, highlight the parameters of relevance to decision making, and include the rationale relied on for the conclusions reached in the light of the weight of evidence provided by the data reported.

(x) Where relevant, an evaluation, cross referenced to the supporting documentary evidence, of the relevance of particular studies conducted regionally, to the agricultural, plant health and environmental (including climatic) conditions of other regions, together with the rationale for extrapolations proposed, should be included.

(xi) Within each section and sub-section, having regard to the data provided, it is necessary that each decision making point be highlighted, having regard to:

- the weight of the evidence available - extent, quality and consistency of the data; and
- the criteria and guidelines for evaluation and decision making currently used in the country to which application is made.

3.2 Dossier on the MPCP

3.2.1 Tier I - Document L (MPCP)

- Checks as to the acceptability of the quality of individual test and study reports relating to the MPCP

(I) The dossier summary should, in principle, include a report as to the acceptability of the quality of each individual test and study submitted to address each point of the data requirements. Those reports should be compiled in Sections as specified in subparagraph (xviii).

(ii) Where application is made for the approval or continued approval of an MPCA, in order to ensure that any approval granted embraces all uses that are being supported, without unnecessary conditions and restrictions, thereby facilitating registration of MPCPs containing the MPCA for all such uses, the number of MPCPs for which a dossier is submitted should be sufficient to reflect the types of MPCPs and applications envisaged, as well as worst case scenarios for operator, worker and environmental exposure.

(iii) The Tier I checks as to the acceptability of the quality of individual test and study reports to be submitted are intended to facilitate efficiency in the use of the resources available to the regulatory authorities for the evaluation of dossiers (scientific secretariats and specialist evaluators). In particular they are intended to facilitate the checking of dossiers as to completeness and format, checks to ensure compliance with the principles of GLP or GEP, as appropriate and, checks relating to the suitability of test methods used.

(iv) In the case of testing as to the identification and biological properties of MPCPs and by way of exception, it is not necessary that reports as to the quality of individual tests be provided. Details of the methodologies used should be provided in the Tier II summary (see paragraph 3.2.2) and instances of non-compliance with or, of divergence or omissions from the requirements relating to the principles of GLP or GEP, as appropriate, should be indicated and be justified for each individual test or study.

(v) Efficacy data and information must be submitted in support of applications for the registration of individual MPCPs in many but not all countries. It is not necessary, that reports as to the quality of individual tests and trials be provided. Details of the methodologies used should be provided in the Tier II summary (see paragraph 3.2.2) and instances of non compliance with or, of divergence or omissions from the requirements relating to the principles of GEP should be indicated and be justified for each individual test or trial.

(vi) Where the test methods used were those currently specified, and where the tests or studies concerned were conducted in accordance with the principles of GLP/GEP, as appropriate, Tier 1 checks as to the acceptability of the quality of individual test and study reports should take the following form (examples are provided in Part 1 of Appendix 4):

1.1 the data point addressed (cf subparagraph xviii),
1.2 a description of the type of test or study;
2 reference point (location) of the report in the dossier (e.g. section 3, point 7.1.4 /01);
3.1 the names of the authors,
3.2 the title of the test or study report,
3.3 the owner of the report,
3.4 an indication as to whether it is a published or unpublished report,
3.5 the report number,
3.6 the date of the report;
4.1 the name and address of the testing facility,
4.2 the laboratory report/project number;
5 the dates of commencement and completion of experimental work;
6.1 the identity of the test substance or material (brand name, batch number and degree of purity),
6.2 an explicit reference to the relevant specification of composition of the test substance or material;
7.1 the identity of the test guideline used,
7.2 where test guidelines provide choice as to the method to be used, a reasoned justification for the method used;
7.3 where deviations from the test guidelines specified are employed, a description of and reasoned justification for the deviations;
8 confirmation that the principles of GLP or GEP, as appropriate, were complied with - in the event of non-compliance a description of the degree of non-compliance and a justification for non-compliance.

(vii) For tests and studies for which the test methods used were not those currently specified (i.e. studies conducted in accordance with test guidelines which have been replaced or were never accepted), a more detailed approach is necessary in which each of the

following points should be addressed in the Tier 1 checks as to the acceptability of the quality of individual test and study reports - where a particular heading is not relevant, the reason that it is not relevant should be stated. Please see Appendix 11, Form 5.

(viii) The suggested format for the presentation of Tier I checks as to the acceptability of the quality of individual test and study reports for tests and studies on MPCPs is the same as that for tests and studies relating to MPCAs as presented in Part 2 of Appendix 4.

(ix) It is not necessary that Tier I checks as to acceptability of the quality of reports be provided for reports relating to analytical methods, identification and biology.

(x) The final part of Tier I of the summary dossier should comprise a listing of all test and study reports, test guidelines, and published papers, submitted as part of the dossier and a separate listing of all test and study reports, test guidelines, and published papers, not submitted as part of the dossier, of which the applicant is aware and which are relevant to the regulatory decision proposed (i.e. those that address relevant end-points). It is to be noted that applicants are obliged to submit all relevant information of which they are aware concerning potentially dangerous effects, not just a reference to such reports and papers

iv. In preparing the listing, applicants should conduct a detailed literature search - expert judgement is required to determine the nature and extent of the search to be conducted. The date on which the reference list was compiled, the identity of the data bases searched, the date range established for the purposes of the search (e.g. abstracts dated earlier than 1980 not requested), the language constraints, if any, imposed and the key words used for the purposes of the literature search, should be indicated.

i. The listing of test and study reports, test guidelines, and published papers submitted as part of the complete dossier, should cover each section of the dossier separately. References which relate to more than one section should be listed in each relevant section. Within sections, for each point, and where appropriate, sub-point, the list should be arranged alphabetically by author. Where for a particular author there is more than one report or paper, they should be listed in chronological order, with the most recent report or paper listed last. In cases where for a particular author, more than one reference is listed for any one year, the references should be distinguished by inserting letters after the year i.e. a, b, c, etc., as appropriate. For each test and study report, an indication should be provided as to whether or not it is published and as to whether or not it was conducted in compliance with the principles of GLP or the principles of GEP, as appropriate. The listing of individual test and study reports should be annotated to indicate their owner and to indicate whether or not data protection is claimed in accordance with the relevant rules or provisions in place in the country to which the dossier is submitted. Before regulatory decisions are made, applicants will be required, where appropriate, to certify that the studies for which they have claimed data protection, have or have not been submitted in support of other applications. A suggested format for the presentation of the listings of test and study reports, test guidelines, and published papers submitted is contained in Part 1 of Appendix 6. In order to facilitate the subsequent manipulation of the reference list by the regulatory authority to which it is submitted, the listing should be compiled using a word processing table function, using a separate row for each reference

ii. second version of the listing of test and study reports, test guidelines, and published papers, submitted as part of the complete dossier, which should again cover each section of the dossier separately, but in which the tests and studies are listed alphabetically by author and for individual authors, in chronological order, should be provided. A suggested format for the presentation of the second listing of test and study reports, test guidelines, and published papers submitted is contained in Part 2 of Appendix 6. In order to facilitate the subsequent manipulation of the reference list by the regulatory authority to which it is

submitted, the listing should be compiled using a word processing table function, using a separate row for each reference.

iii. In the case of test and study reports and published papers not submitted, a separate listing of such documents, arranged alphabetically by author, should be provided at the end of each section. A suggested format for the presentation of the listings of test and study reports and published papers not submitted is contained in Part 3 of Appendix 6. In order to facilitate the subsequent manipulation of the reference list by the regulatory authority to which it is submitted, the listing should be compiled using a word processing table function, using a separate row for each reference.

iv. The separate sections for which a listing of test and study reports, test guidelines, and published papers is required are as follows:

Section 1

- Identity of the MPCP,
- Identification and physical/chemical properties of the MPCP,
- Data on application (field of use; effects on harmful organisms; details of intended use - harmful organisms controlled and/or plants or plant products to be protected; application rate; concentration of MPCA in material used; method of application; number and timing of applications and duration of protection; necessary waiting periods or other precautions to avoid phytotoxic effects on succeeding crops; proposed instructions for use),
- Further information on the MPCP (packaging details and compatibility of the preparation with proposed packaging materials; procedures for cleaning application equipment; re-entry periods, necessary waiting periods or other precautions to protect man, livestock and the environment; recommended methods and precautions concerning handling, storage, transport or fire; emergency measures in the case of an accident; procedures for destruction or decontamination of the MPCP and its packaging), and
- Proposals including justification for the classification and labelling (risk and safety phrases) of the MPCP, and
- Proposed label for the MPCP
- manufacturers methods for the MPCP; quality control information for the MPCP

Section 2 Analytical methods;

Section 3 Health studies

Section 4 Residues (normally not required)

Section 5 Fate and behaviour in the environment;

Section 6 Ecotoxicological studies and risk assessment; and

Section 7 Efficacy data and information (effectiveness; resistance; effects on the quality of plants and plant products; effects on yield of treated plants or plant products; phytotoxicity to target plants or plant products; economics; benefits).

v. For the purposes of avoiding confusion and facilitating the examination of dossiers submitted, a compilation of all scientific name of microorganism to species level or a level sufficient to show taxonomic relation to known microorganisms, especially pathogens; accession no. of sample in a recognized culture collection; test procedures and criteria, using best

available technology, to characterize the strain or serotype; for mutant or genetically-modified strains (For EU Member States, please refer to Dir 90/219 and Dir 90/220 for submissions to EU countries that contain genetically engineered organisms), indicate all known differences between the modified microorganism and the parent wild strain(s)- include any trade names, common names, and developmental code names The approach suggested for the preparation of compilations of names, synonyms and code names for MPCAs is illustrated in the listing comprising Part 4 of Appendix 1.

vi. The numbering systems used in many OECD countries for the data and information relating to MPCPs to be submitted, are different. Applicants should use the OECD numbering system which may be found in Part 5 of Appendix 6 for submitting data and information appropriate to the country (or countries) to which application(s) is (are) being made. Alternatively, applicants can use the country-specific numbering system for the country to which application is being made. A compilation of the numbering systems used in some OECD countries is included in Part 5 of Appendix 6.

(xvii) The OECD numbering system for the data and information to be submitted provides in a number of cases for flexibility as to whether particular studies are submitted as part of the dossier on the MPCA or as part of the dossier on the MPCP. That flexibility, within the constraints imposed by the regulatory requirements of the country or countries to which submission is to made, is intended to accommodate applicant preferences. Regardless of the choices made by applicants, it is necessary that suitable cross references be provided, as appropriate.

3.2.2 Tier II - Document M (MPCP) - Summary and assessment of the dossier relating to the MPCP

vii. The Tier II summary for a MPCP should contain sections such that it contains a discussion and interpretation of the results of all tests and studies relating to the MPCP and within each section, the conclusions reached. The sections are those listed in paragraph 3.2.1 (xviii).

i. Where relevant and necessary (e.g. registration of a MPCP) the final section (Section 7 - Efficacy) should be included. The separate elements to be addressed in the section on efficacy include effectiveness, potential for the development of resistance, effects on the quality of plants and plant products, effects on yield of treated plants or plant products and phytotoxicity to target plants or plant products). Guidelines for the preparation and presentation of efficacy data have been issued by some countries e.g. European Union [3].

ii. Tier II summaries, which should consist of a discussion and interpretation of the results of the tests and studies contained in the dossier for the MPCP provided, for the purposes of that discussion and interpretation, should draw on data and information contained in the relevant MPCA dossier(s).

iii. In the case of non submission of particular studies, full justifications should be provided. (See Appendix 2, and Appendix 11, Part 4)

iv. Where the principles of GLP or GEP have not been followed, or where the methodologies used were not those currently prescribed in the country to which application is being made or, where there were deviations from the methods prescribed or other methods used, a justification of the overall quality and scientific validity of the test or study reported should be provided.

v. As a general rule, a concise but comprehensive summary of each individual test and study should be included. Each summary should include the following elements, as appropriate:

- the reference number of the test or study;
- the appropriate test or study reference (e.g. Casida et al 1979);
- the test guideline and method used;
- relevant GLP/GEP information;
- a brief description of the methodology used;
- a concise tabular presentation of the findings with supporting text in which the significance of results obtained, effects and observations reported, are highlighted; and
- conclusions reached (to be highlighted);

vi. By way of exception to the general rule, in the case of certain parts of the dossier such as Section 1, a tabular approach to the presentation of the data may be appropriate.

(viii) Examples of parts of an Tier II summary are provided in Appendix 8:

3 Commission Document 7600/VI/95, rev 6 of 14 July 1997, Guidelines and criteria for the preparation and presentation of data concerning efficacy as provided in Annex III, parts A and B, section 6 of Directive 91/414/EEC concerning the placing of MPCPs on the market (biological assessment dossier)

- Part 1 contains an example of that part of a Tier II summary which relates to the identity of the MPCP, identification and physical/chemical properties of the MPCP; methods of analysis; and further information on the MPCP;
- Part 2 contains an example of a Tier II summary relating to health studies;
- Part 4 contains an example of a Tier II summary relating to efficacy testing; and
- Part 5 contains an example of a data waiver regarding residues

vii. For each of the Sections of the Tier II summary, it is particularly important that the concluding element for each point and the concluding element of sub-sections and sections, highlight the parameters of relevance to decision making, and include the rationale relied on for the conclusions reached in the light of the weight of evidence provided by the data reported.

i. Where relevant, an evaluation, cross referenced to the supporting documentary evidence, of the relevance of particular studies conducted regionally (e.g. rate of degradation in soil), to the agricultural, plant health and environmental (including climatic) conditions of other regions, together with the rationale for extrapolations proposed, should be included.

ii. Within each section and sub-section, having regard to the data provided, it is necessary that each decision making point be highlighted, having regard to:

The weight of the evidence available - extent, quality and consistency of the data; and

- the criteria and guidelines for evaluation and decision making currently used in the country to which application is made.

3.3 Overall Summary and Assessment - Tier III - Document N (MPCA and MPCP)

3.3.1 This, the final evaluation level, should involve an integration of the results obtained and conclusions drawn on the basis of the tests, studies and information provided relating to both the MPCAs and the MPCPs. The order in which the various elements should be presented is indicated in Table 1.

3.3.2 The Tier III overall summary and assessment should contain a concise summary of the data base presented in the MPCA and MPCP dossiers. That summary should be supported with a detailed statement of the applicant's overall assessment of the dossier, and should contain a reasoned statement of the conclusions which the applicant believes should be reached on the basis of the data and information provided, having regard to:

- the weight of the evidence available - the extent, quality and consistency of the data;
- the criteria and guidelines for evaluation and decision making currently used in the country to which application is made.

3.3.3 The assessment of the data base provided, should establish the rationale for the decision to be taken. It is especially important that the overall assessment of the data base prepared include details of the conditions and restrictions to be associated with any approval or registration to be granted, together with a detailed justification for the proposals made. A listing of all end points which are used in or are relevant to the proposed decision should be appended to the Tier III overall summary and assessment. In order to ensure a consistent approach in preparing the listing of end points, the format illustrated in Appendix 9 should be used.

3.3.4 An example of a Tier III summary and overall assessment is provided in Appendix 10.

Table 1. Order in which the reasoned statement of the conclusions reached by the applicant are to be presented

Chapter 1	The MPCA, its properties, uses, proposed classification and labelling
1.1	Identity
1.2	Biological and technical properties
1.3	Details of uses and further information
1.4	Classification and labelling
1.5	manufacturers methods for the MPCA; quality control information for the MPCA
Chapter 2	Methods of analysis
2.1	method of identification of MPCA and metabolites (especially toxins)
2.2	for MPCP analysis
Chapter 3	Impact on human and animal health
3.1	Effects having relevance to human and animal health arising from exposure to the MPCA or to impurities contained in the MPCA or to their transformation products
Chapter 4	Residues (normally not required)
Chapter 5	Fate and behaviour in the environment
5.1	Persistence in the environment
Chapter 6	Effects on non-target species
6.1	Effects on terrestrial vertebrates
6.2	Effects on aquatic species
6.3	Effects on bees and other arthropod species
6.4	Effects on earthworms and other soil macro-organisms
6.5	Effects on soil micro-organisms
6.6	Effects on other non-target organisms (flora and fauna)
6.7	Environmental risk mitigation
Chapter 7	Efficacy data and information
7.1	Effectiveness
7.2	Information on the occurrence or possible occurrence of the development of resistance
7.3	Effects on the yield of treated plants or plant products in terms of quantity and/or quality
7.4	Phytotoxicity to target plants (including different cultivars), or to target plant products
7.5	Observations on undesirable or unintended side effects e.g. on beneficial and other non-target organisms, on succeeding crops, other plants or parts of treated plants used for propagating purposes (e.g. seeds, cuttings, runners)
7.6	Economics
7.7	Consideration of benefits
Final Chapter	Overall conclusions
	Proposed decision
	Further information to be submitted

4 CHECKING OF DOSSIERS FOR COMPLETENESS

4.1 Introduction

The guidance and forms provided herewith, are for use in checking dossiers for completeness, whether such dossiers are to be submitted in support of an application for approval of a MPCA for the registration of a MPCP, or in the context of the review or renewal of any such approval, registration. It is intended that the forms be completed by applicants and be submitted as part of the application submitted (Document O).

4.2 Suggested Approach

4.2.1 The nature and extent of the check for completeness should be such that it is confirmed that:

(I) all the required supporting documentation has been included (Documents A to J);

(ii) the Tier I checks as to the acceptability of individual test and study reports, the Tier II dossier summaries and assessments and the Tier III overall summary and assessment, have been included;

(iii) all test and study reports relating to the MPCA required in accordance with the requirements specified for the country to which application is made (Document K MPCA) or, in the case of particular test and study reports, either a justification for non provision, or an undertaking to provide them at a future specified date, have been provided; and

(iv) all test and study reports relating to the MPCP required in accordance with the requirements specified for the country to which application is made (Documents K - MPCP) or, in the case of particular test and study reports, either a justification for non provision, or an undertaking to provide them at a future specified date, have been provided.

4.2.2 Some of The forms necessary for checking dossiers for completeness are provided in Appendix 11.

Evaluation Form 1	for use in checking that the required supporting documentation has been provided	Appendix 11, Part 1
Evaluation Form 2	for use in checking that the required MPCA and MPCP product dossier summaries and an overall assessment, have been provided	Appendix 11, Part 2
Evaluation Form 3	for use in checking that all test and study reports relating to the MPCA which are required, have been provided	Appendix 11, Part 3
Evaluation Form 4	for use in checking that all test and study reports relating to the MPCP which are required, have been provided	Appendix 11, Part 4

4.2.3 A completed set of evaluation forms 1, 2, 3 and 4 (Document O - hard copy and/or diskette) must accompany each dossier submitted. The completed forms will be used, by the regulatory authority of the country to which application is made, in conducting its initial evaluation of the dossier to check it for completeness.

4.2.4 Although it is not necessary that completed forms be submitted, forms and supporting documentation for use in checking the acceptability of the quality of individual test and study reports, are also provided in Appendix 11 -

Evaluation Form 5	for use in checking that the Tier I quality checks for individual test and study reports, conducted in accordance with test methods other than those currently specified, are themselves of acceptable quality.	Appendix 11, Part 5
Supporting document	Listing of the test guidelines specified and the requirements relating to compliance with GLP and GEP for individual tests and studies relating to the MPCA	regulatory authorities of individual countries
Supporting document	Listing of the test guidelines specified and the requirements relating to compliance with GLP and GEP for individual tests and studies relating to the MPCP	regulatory authorities of individual countries