OECD Guidance for Industry Data Submissions on Plant Protection Products and their Active Substances

(Dossier Guidance)

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 2, May 2005 -

- OECD Environment Directorate -

FOREWORD

This document is intended to provide guidance to applicants wishing to have particular active substances approved or plant protection products registered. It provides guidance with respect to the format and presentation of the documentation to be submitted. The guidance provided is also relevant to the documentation to be submitted in support of proposals for the establishment of Maximum Residue Limits (MRLs) and/or Import Tolerances as well as to any documentation to be submitted by other interested parties wishing to have other information taken into account by the relevant regulatory authorities. 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 active substances in Annex I of Directive 91/414/EEC (Article 5.3 and 8.2), 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 active substance 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 individual study summaries include more headings and sub-headings and include an executive summary.

This document was first approved by the 7th Meeting of the Working Group on Pesticides that took place in February 1998 at the Château de la Muette, Paris, and endorsed by the Joint Meeting of the Chemicals Committee and Working Party on Chemicals, Pesticides and Biotechnology in June 1998. New and revised parts, dated August 1999, were approved by the 8th Meeting of the Working Group on Pesticides that took place in June 1999, those dated March 2001 were approved by the 11th Meeting of the Working Group that took place in November 2000, while those dated May 2005 were approved by the 17th Meeting of the Working Group that took place in November 2004.

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/ehs/pesticid.htm or contact the OECD Secretariat to make sure that you have the latest version.

Pesticide Programme
Health and Safety Division
Environment Directorate
Organisation for Economic Co-operation and Development
2, rue André Pascal
75775 Paris Cedex 16
France

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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 active substances, for the registration of a plant protection product, for the establishment of a maximum residue limit (MRL) or limits, for the establishment of an import tolerance or tolerances, or in the context of the review or renewal of any such approval, registration, MRL or import tolerance. 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 active substances, plant protection products, or their residues, on human or animal health or the environment.

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 an active substance, for the registration or re-registration of a plant protection product, for the establishment of an MRL or MRLs, for the establishment of an import tolerance or tolerances, 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 Standard Abbreviations - in the interest of avoiding confusion, standard technical terms and abbreviations as specified in Appendices 1 and 2, must be 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;

1. Particular attention is drawn to the requirement to use metric units - *e.g.* in the case of application rates, kg active substance/ha; content of active substance in formulations, g/kg or g/l; content of residues, mg/kg; doses in feeding studies, mg/kg body weight. If non metric units are used, metric equivalents or conversion factors to metric units must be provided.

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 European Crop Protection Association (ECPA):

European Crop Protection Association
Avenue E. van Nieuwenhuyse
B-1160 Brussels
Belgium
Phone: 32 2 663 15 50
Fax: 32 2 663 15 60
WWW: http://www.ecpa.be/

Regardless of the option chosen, applicants are encouraged, where possible, to present information in tabular form (*e.g.* GAP Tables (Documents D1 and D2), MRL lists (Documents E1 and E2), reference lists). 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 active substance, for the registration or re-registration of a plant protection product, for the establishment of an MRL or of MRLs, for the establishment of an import tolerance or tolerances, or a proposal to vary the conditions of any such registration, or relates to the review of any such registration, MRL or import tolerance, 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 active substance,
- approval of an existing active substance,
- registration of a plant protection product containing a new active substance,
- registration of a plant protection product containing an existing active substance,
- modification or removal of conditions or restrictions associated with the registration of a plant protection product,
- special review of the registration of a plant protection product, where indications exist suggesting that the conditions of registration are no longer satisfied,
- routine review of the registration of a plant protection product, anticipating expiryof the period for which registered,
- establishment of an MRL or of an import tolerance, or
- renewal of an MRL or of an import tolerance;

Document B Task Force Information

where relevant, details of any task force that exists or is formed for the purposes of defending particular active substances. 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, registration or MRL (Document D-1) - 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 active substances, 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 plant protection product for which the product is not currently commercialized; uses for which the maximum registered application rate is seldom if ever availed of);

Document D-3 Supported Uses in Exporting Countries

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 which are imported in significant quantities into the territory of the country to which application is made and for which import tolerances are required (Document D-3) - the information concerned should be provided using forms as set out in Part 1 of Appendix 3;

Document E-1 Existing MRLs

where they exist, a listing of the MRLs established for the active substance in the country to which application is made, together with a listing of MRLs established by the CAC or proposed by the CCPR, together with the associated residue definitions, should be provided (Document E-1) using forms as set out in Part 3 of Appendix 3;

Document E-2 MRLs in Exporting Countries

where an import tolerance is required, a listing of the MRLs established for the active substance in countries that export the plants and plant products concerned and in addition, where relevant, a listing of MRLs and import tolerances established in other OECD countries, together with the associated residue definitions, should be provided (Document E-2) using forms as set out in Part 3 of Appendix 3;

Document F **Statements of Intention to Submit a Dossier**

where in the case of the review of existing registrations, MRLs or import tolerances, 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 active substance), the following -

Document G ● a 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 H ● a 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 active substance 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 K (active substance) **Test and Study Reports**

Document K (formulation) 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 active substance and formulated products. Where the registration of more than one formulation is requested, a separate dossier on each plant protection 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 (active substance) (*Tier I*)
Document L (formulation)
Document L (reference lists)

- 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,

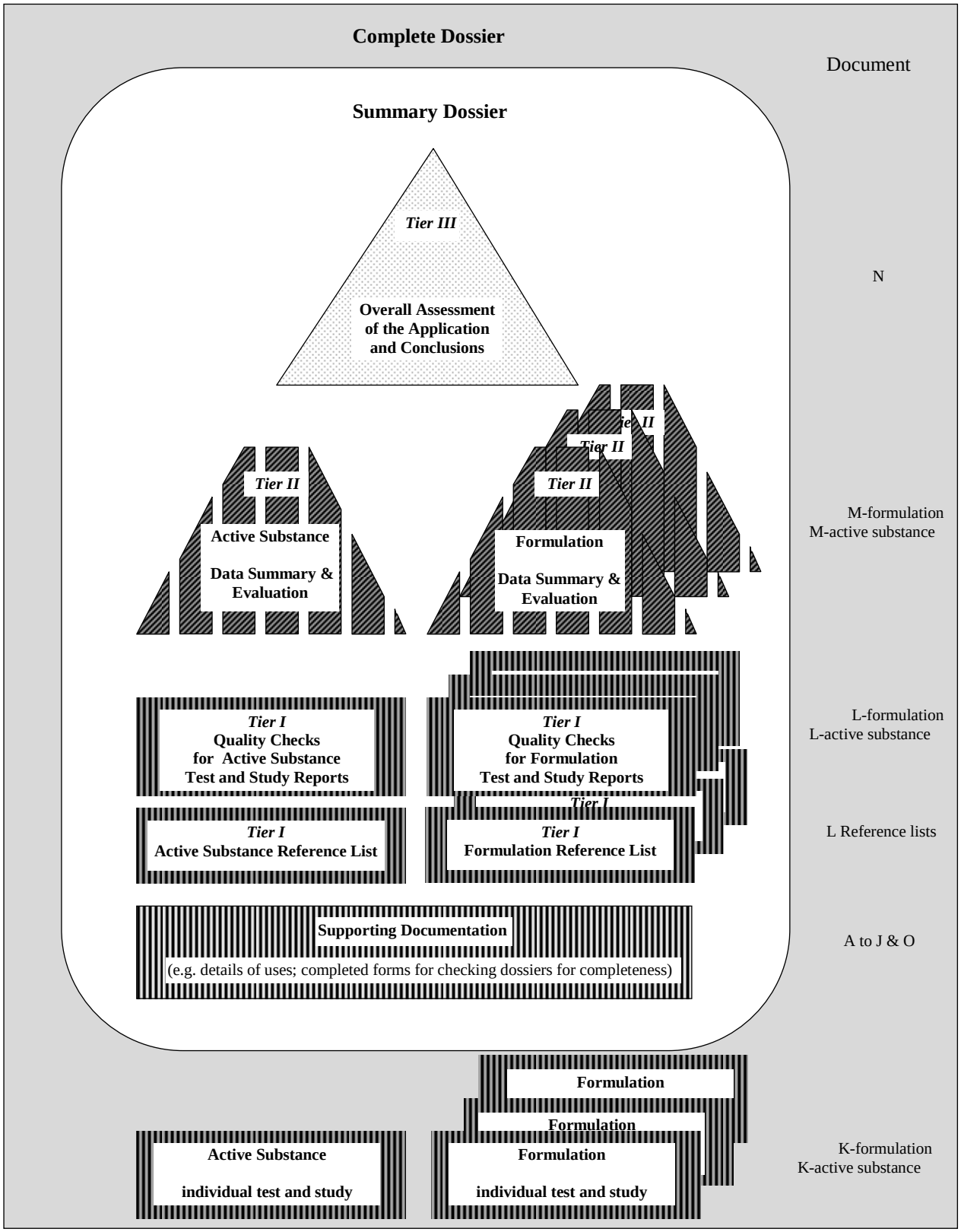
Document M (active substance) (*Tier II*)
Document M (formulation)

- 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,

Figure 1

DOSSIER STRUCTURE AND CONTENT



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).

2.3 Samples and Analytical Standards

Where requested, a sample of each active substance as manufactured and which complies with the specification(s) submitted, together with analytical standards for each component included in the proposed residue definition and of analytical standards for inactive isomers and impurities of toxicological or environmental concern present in significant quantities in the active substance as manufactured, should be provided.

3 DOSSIER SUMMARIES AND OVERALL ASSESSMENTS - DETAILED REQUIREMENTS

3.1 Dossier on the active substance

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

(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 relevant data requirement. Those reports should be assembled in six Sections as specified in subparagraph (xv).

(ii) 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. Except as specified here under for supervised residue trials and for soil dissipation studies (subparagraphs viii and ix), a summary of the findings or experimental results obtained, should not be included in *Tier I*.

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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 formulations, efficacy and phytotoxicity tests)

(iii) In the case of testing as to the physical and chemical properties of active substances 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.

(iv) 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 xvii),
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 (ISO common 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.

(v) 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:

1.1 the data point addressed (*cf* subparagraph xvii),
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 5.2.2 /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;

5.1 the dates of commencement and completion of experimental work,
5.2 a statement of the objectives of the test or study;

6.1 the identity of the test substance or material (ISO common name, batch number and degree of purity),
6.2 an explicit reference to the relevant specification of composition of the test substance or material,
6.3 where available, data relevant to the storage stability of the test substance or material,
6.4 where relevant and available, data as to the stability of the test substance or material in the dosing vehicle,
6.5 where relevant and available, data as to the homogeneity of the test substance or material in the dosing or testing vehicle,
6.6 where data relating to the stability or homogeneity of the test substance is not available (*e.g.* certain older studies), a justification of the scientific validity of the study,
6.7 where relevant, information as to the physical form of the test substance or material,
6.8 full details of the composition of any dosing vehicles or solvents used;

7.1 the identity of the test method used,

7.2 where not a method specified, a reasoned justification for the choice of method used in terms of its scientific validity and comparability with the method currently specified,
7.3 on request, a copy of the method - full details of methods used which are unlikely to be accessible to the regulatory authority of the country to which the dossier is submitted, should be attached to the study or test report,
7.4 where test guidelines provide choice as to the method to be used, a reasoned justification for the method used,
7.5 where deviations from the test guidelines specified, or from other methods used, are employed, a description of and reasoned justification for the deviations;

8.1 where relevant, an indication as to whether, or not, the test or study has been conducted by a laboratory certified as to its competence to conduct the test or study in compliance with the principles of GLP,
8.2 where relevant, the certifying authority,
8.3 where applicable, an indication as to whether, or not, the principles of GLP have been complied with,
8.4 where relevant, a justification for non compliance with the principles of GLP;

9.1 where relevant, a clear statement as to whether, or not, the test or study was conducted in accordance with the principles of GEP,
9.2 where conducted in accordance with the principles of GEP, whether conducted by an official or an officially recognized testing facility or organization,
9.3 where relevant, a justification for non compliance with the principles of GEP;

10 a description of the test system;

11 the identity of any statistical and other techniques applied to the data to aid interpretation, together with adequate documentation thereof and a justification for the use of the technique selected where non standard techniques are used;

12.1 where reference to published papers is made in *Tier I* quality checks, the bibliographic references concerned,

12.2 copies of the papers concerned; and

13 where reference to unpublished data is made in *Tier I* quality checks (*e.g.* historical control data on strains of test animals) a summary of such data.

(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, regardless of whether the methods concerned relate to residues analysis, analysis of active substance as manufactured or analysis of formulations. 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).

(viii) By way of further exception to the general rule, summaries of individual supervised residue trials, rather than checks **as to the acceptability of the quality of individual study reports**, should be provided. For the purposes of compiling such *Tier I* summaries, the forms as contained in Part 1 of Appendix 5, should be used. Trials data relevant to all GAPs for which MRLs exist or are proposed, should be included. Where an import tolerance is required, trials data relevant to all GAPs for which the import tolerance is required must also be included. The forms concerned should be grouped by crops and within crops by the country in which trials were conducted.

(ix) A similar approach should be taken with respect to soil dissipation studies. In preparing *Tier I* summaries of soil dissipation studies, the forms as contained in Part 2 of Appendix 5, should be used.

(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.

(xi) 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.

(xii) 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 spreadsheet programme, using a separate row for each reference.

(xiii) 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 spreadsheet programme, using a separate row for each reference.

(xiv) 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 spreadsheet programme, using a separate row for each reference.

(xv) 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 active substance,
- Physical and chemical properties of the active substance,
- Further information on the active substance (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),
- Proposals including justification for the proposals for the classification and labelling of the active substance;

Section 2 Analytical methods;

Section 3 Toxicological and metabolism studies on the active substance;

Section 4 Residues in or on treated products, food or feed (nature of the residue, level of residue and consumer risk assessment);

Section 5 Fate and behaviour in the environment; and

Section 6 Ecotoxicological studies on the active substance.

(xvi) For the purposes of avoiding confusion and facilitating the examination of dossiers submitted, a compilation of all chemical names, common names, synonyms and code names, used for the active substance and its metabolites should be appended to *Tier I* of the summary dossier. For each

compound, its chemical name followed by all other names used, should be listed. The approach suggested for the preparation of compilations of chemical names, common names, synonyms and code names for active substances and metabolites is illustrated in the listing comprising Part 3 of Appendix 1.

(xvii) The numbering systems used in many OECD countries for the data and information relating to active substances 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 active substance or as part of the dossier on the formulated product. 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 (active substance) - Summary and assessment of the dossier relating to the active substance

(i) The *Tier II* summary for an active substance should contain six sections such that it contains a discussion and interpretation of the results of all the tests and studies which relate to the active substance and within each section, the conclusions reached. The six sections are those specified in paragraph 3.1.1 (xv).

(ii) Where relevant and necessary (*e.g.* registration of a plant protection product, rather than the establishment of an MRL or import tolerance), efficacy data and information is required in some countries. However, such information is relevant to the formulation rather than to the active substance. It therefore is neither necessary nor appropriate that the *Tier II* summary for the active substance include such information.

(iii) The *Tier II* summary should be confined to and rely only on that data and information contained in the active substance 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.

(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 *physical and chemical properties of the active substance*, and that relating to *residue trials* (supervised residue trials) a tabular approach to the presentation of the data may be appropriate, while in the case of metabolism studies (animals, plants and soil) and soil dissipation studies, it may be more convenient to provide summaries of groups of tests and studies. In the case of supervised residues trials data, it is necessary that, where relevant, a clear statement be included to indicate the differences, if any, in the data base included in comparison to that presented by the applicant to the JMPR for the purposes of the elaboration of CAC MRLs.

(viii) Examples of parts of a *Tier II* summary for an active substance are provided in Appendix 7 - Part 1 contains the suggested format for that part of a *Tier II* summary which relates to the *physical and chemical properties of the active substance*, Part 2 contains the suggested format for part of a *Tier II* summary relating to *analytical methods*, while Part 3 contains an example of part of a *Tier II* summary relating to *toxicological and metabolism studies*. Part 4 of Appendix 7 contains suggestions for the format to be used for the presentation of residue data in summary form - the suggested approach is based on that recommended in the JMPR Manual for FAO Panel Members [3]. An example of part of a *Tier II* summary relating to fate and behaviour in the environment (fate and behaviour in soil), is provided in Part 5 of Appendix 7.

(ix) For each of the six 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 (*e.g.* residue data), 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. Pesticide residues in food - 1994. Report of 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. FAO Plant Production and Protection Paper 127.

3.2 Dossier on the formulated product

3.2.1 Tier I - Document L (formulation) - Checks as to the acceptability of the quality of individual test and study reports relating to the formulated product

(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 seven Sections as specified in subparagraph (xvii).

(ii) Where application is made for the approval or continued approval of an active substance, in order to ensure that any approval granted embraces all uses that are being supported, without unnecessary conditions and restrictions, thereby facilitating registration of formulations containing the active substance for all such uses, the number of formulations for which a dossier is submitted should be sufficient to reflect the types of formulations 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. Except as specified here under for supervised residue trials and for soil dissipation studies (subparagraphs x and xi), a summary of the findings or experimental results obtained, should not be included in *Tier I*.

(iv) In the case of testing as to the physical, chemical and technical properties of formulated products 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 plant protection products 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 xix),
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:

1.1 the data point addressed (*cf* subparagraph xix),
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;

5.1 the dates of commencement and completion of experimental work,
5.2 a statement of the objectives of the test or study;

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,
6.3 where available, data relevant to the storage stability of the test substance or material,
6.4 where relevant and available, data as to the stability of the test substance or material in the dosing vehicle,
6.5 where relevant and available, data as to the homogeneity of the test substance or material in the dosing or testing vehicle,

6.6 where data relating to the stability or homogeneity of the test substance is not available (*e.g.* certain older studies), a justification of the scientific validity of the study,

6.7 where relevant, information as to the physical form of the test substance or material,

6.8 full details of the composition of any dosing vehicles or solvents used;

7.1 the identity of the test method used,

7.2 where not a method specified, a reasoned justification for the choice of method used in terms of its scientific validity and comparability with the method currently specified,

7.3 on request, a copy of the method - full details of methods used which are unlikely to be accessible to the regulatory authority of the country to which the dossier is submitted, should be attached to the study or test report,

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

7.5 where deviations from the test guidelines specified, or from other methods used, are employed, a description of and reasoned justification for the deviations;

8.1 where relevant, an indication as to whether, or not, the test or study has been conducted by a laboratory certified as to its competence to conduct the test or study in compliance with the principles of GLP,

8.2 where relevant, the certifying authority,

8.3 where applicable, an indication as to whether, or not, the principles of GLP have been complied with,

8.4 where relevant, a justification for non compliance with the principles of GLP;

9.1 where relevant, a clear statement as to whether, or not, the test or study was conducted in accordance with the principles of GEP,

9.2 where conducted in accordance with the principles of GEP, whether conducted by an official or an officially recognized testing facility or organization,

9.3 where relevant, a justification for non compliance with the principles of GEP;

10 a description of the test system;

11 the identity of any statistical and other techniques applied to the data to aid interpretation, together with adequate documentation thereof and a justification for the use of the technique selected where non standard techniques are used;

12.1 where reference to published papers is made in *Tier I* quality checks, the bibliographic references concerned,

12.2 copies of the papers concerned; and

13 where reference to unpublished data is made in *Tier I* quality checks (*e.g.* historical control data on strains of test animals) a summary of such data.

(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 formulated products is the same as that for tests and studies relating to active substances, 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, regardless of whether the methods concerned relate to residues analysis, or analysis of formulations.

(x) By way of further exception to the general rule, summaries of individual supervised residue trials, rather than checks as to the acceptability of the quality of individual study reports, should be provided. For the purposes of compiling such *Tier I* summaries, the forms as contained in Part 1 of Appendix 5, should be used. Trials data relevant to all GAPs for which MRLs exist or are proposed, should be included, except where the information concerned has already been provided as part of the dossier relating to the active substance. Similarly, where an import tolerance is required, trials data relevant to all GAPs for which the import tolerance is required

must be included, except where the information concerned has already been provided as part of the relevant dossier relating to the active substance. The forms concerned should be grouped by crops and within crops by the country in which trials were conducted.

(xi) A similar approach should be taken with respect to soil dissipation studies. In preparing *Tier I* summaries of soil dissipation studies, the forms as contained in Part 2 of Appendix 5, should be used.

(xii) 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.

(xiii) 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.

(xiv) 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 spreadsheet programme, using a separate row for each reference

(xv) 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 spreadsheet programme, using a separate row for each reference.

(xvi) 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 spreadsheet programme, using a separate row for each reference.

(xvii) 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 plant protection product,
- Physical, chemical and technical properties of the plant protection product,
- 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 active substance 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 plant protection product (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 plant protection product and its packaging), and
- Proposals including justification for the classification and labelling (risk and safety phrases) of the plant protection product, and
- Proposed label for the plant protection product;

Section 2 Analytical methods;

Section 3 Toxicological studies and exposure information and data (operators - mixers, loaders and applicators; workers; bystanders);

Section 4 Residues in or on treated products, food or feed (nature of the residue, level of residue and consumer risk assessment);

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).

(xviii) For the purposes of avoiding confusion and facilitating the examination of dossiers submitted, a compilation of all chemical names, common names, synonyms, trade names and code names, used for the active substance, preparations containing it and metabolites of the active substance

should be appended to Tier I of the summary dossier. For each compound, its chemical name followed by all other names used, should be listed, while for each preparation its current name followed by all other names used should be listed. The approach suggested for the preparation of

compilations of chemical names, common names, synonyms and code names for active substances, metabolites and formulation is illustrated in the listing comprising Part 3 of Appendix 1.

(xix) The numbering systems used in many OECD countries for the data and information relating to formulated products 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.

(xx) 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 active substance or as part of the dossier on the formulated product. 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 (formulation) - Summary and assessment of the dossier relating to the formulated product

(i) The *Tier II* summary for a plant protection product should contain seven sections such that it contains a discussion and interpretation of the results of all tests and studies relating to the formulation and within each section, the conclusions reached. The seven sections are those listed in paragraph 3.2.1 (xvii).

(ii) Where relevant and necessary (*e.g.* registration of a plant protection product, rather than the establishment of an MRL or of an import tolerance), 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 [4].

(iii) *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 formulated product provided, for the purposes of that discussion and interpretation, should draw on data and information contained in the relevant active substance dossier(s).

(iv) In the case of non submission of particular studies, full justifications should be provided.

(v) 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.

4. 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 plant protection products on the market (biological assessment dossier)

(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 Section 1 and that relating to *residue trials* (supervised residue trials), a tabular approach to the presentation of the data may be appropriate, while in the case of metabolism studies (animals, plants and soil) and soil dissipation studies, it may be more convenient to provide summaries of groups of tests and studies. In the case of supervised residues trials data, it is necessary that, where relevant, a clear statement be included to indicate the differences, if any, in the data base included in comparison to that presented by the applicant to the JMPR for the purposes of the elaboration of CAC MRLs.

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

- Part 1 contains an example of that part of a *Tier II* summary which relates to *the identity of the plant protection product*; *physical, chemical and technical properties of the plant protection product*; *data on application*; and *further information on the plant protection product*;
- Part 2 contains an example of a *Tier II* summary relating to *toxicological studies and exposure information and data*;
- Part 3 contains an example of a *Tier II* summary relating to *ecotoxicological studies and risk assessment*; and
- Part 4 contains an example of a *Tier II* summary relating to *efficacy testing*.

(ix) The format described in Part 4 of Appendix 7 is that proposed for the presentation of residue data in summary form - the suggested approach is based on that recommended in the JMPR Manual for FAO Panel Members [5].

(x) For each of the seven 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.

(xi) 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.

5. See footnote 3, page 16

(xii) 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 (active substance and formulated product dossiers) - Tier III - Document N

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 active substance(s) and the formulated product(s). 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 active substance and formulated product 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 *Tier III* overall summary and assessment prepared, should where relevant, include a diagrammatic representation of the metabolic pathway(s) for the active substance in animals, plants, soil and water. The molecular structure of the active substance and its metabolites, degradation and reaction products should be shown. Major pathways should be distinguishable from minor pathways, which in turn should be distinguishable from possible or suspected pathways.

3.3.4 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.

3.3.5 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 active substance, its properties, uses, proposed classification and labelling
	1.1	Identity
	1.2	Physical and chemical properties
	1.3	Details of uses and further information
	1.4	Classification and labelling
Chapter 2		Methods of analysis
	2.1	for analysis of the active substance as manufactured
	2.2	for formulation analysis
	2.3	for residue analysis
Chapter 3		Impact on human and animal health
	3.1	Effects having relevance to human and animal health arising from exposure to the active substance or to impurities contained in the active substance or to their transformation products
	3.2	Toxicological end point for assessment of risk following long-term dietary exposure - ADI
	3.3	Toxicological end point for assessment of risk following acute dietary exposure – ArfD (acute reference dose)
	3.4	Toxicological end points for assessment of occupational and bystander risks – AOEL / MOE
	3.5	Drinking water limit
	3.6	Impact on human or animal health arising from exposure to the active substance or to impurities contained in it
Chapter 4		Residues
	4.1	Definition of the residue relevant to MRLs
	4.2	Residues relevant to consumer safety
	4.3	Residues relevant to worker safety
	4.4	Proposed MRLs and compliance with existing MRLs
	4.5	Proposed import tolerances and compliance with existing import tolerances
	4.6	Basis for differences, if any, in conclusions reached having regard to established or proposed CAC MRLs
Chapter 5		Fate and behaviour in the environment
	5.1	Definition of the residue relevant to the environment
	5.2	Fate and behaviour in soil
	5.3	Fate and behaviour in water
	5.4	Fate and behaviour in air

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	Effects on biological methods of sewage treatment
	6.8	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 an active substances for the registration of a plant protection product, for the establishment of a maximum residue limit (MRL) or limits, for the establishment of an import tolerance or tolerances, or in the context of the review or renewal of any such approval, registration, MRL or import tolerance. 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 active substance required in accordance with the requirements specified for the country to which application is made (Document K active substance) 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 formulated product required in accordance with the requirements specified for the country to which application is made (Documents K formulation) 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. Other forms necessary for that purpose, as indicated here under, have been developed, or are to be developed by the regulatory authorities of individual countries, or groups of countries (*e.g.* EU), as appropriate:

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 active substance and formulated 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 active substance which are required, have been provided	regulatory authorities of individual countries

Evaluation Form 4	for use in checking that all test and study reports relating to the formulated product which are required, have been provided	regulatory authorities of individual countries

4.2.3 A completed set of evaluation forms 1, 2, 3 and 4 (Document O - hard copy and 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 3
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 active substance	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 formulated product	regulatory authorities of individual countries